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## ANTIBODY RESPONSE TO A STIMULATING DOSE OF TETANUS TOXOID IN CHILDREN PREVIOUSLY IMMUNIZED WITH COMBINED DIPHTHERIA AND TETANUS TOXOIDS (C.D.T.).


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IN a previous paper (North and Patterson, 1953*a*) reference was made to the satisfactory antitoxin response obtained in infants three weeks after a second injection of combined diphtheria and tetanus toxoids.

The investigation reported here is concerned with the estimation of the level of tetanus antitoxin in the serum of children who six months previously had received two doses of combined diphtheria and tetanus toxoids (C.D.T.), and with an analysis of the antibody response of these children to a third or "booster" dose of different antigens containing tetanus toxoid.

### Method and Materials.

Sixty-four children between the ages of nine and sixteen years, the majority of whom had been previously immunized against diphtheria, were given two injections each of 0·5 millilitre of C.D.T. with an interval of six weeks between doses. Six months after the second dose of C.D.T. blood was taken from the children and they were divided into six groups. Immediately after the blood was taken the children in the different groups were given a subcutaneous "booster" dose of a preparation containing tetanus toxoid as follows: Group I received 0·25 millilitre of C.D.T., and group II received 0·5 millilitre of C.D.T. The antigens used for these two groups were the same as those used for the original course of two injections. They contained 25 Lf. of purified diphtheria toxoid, five Lf. of purified tetanus toxoid, and 10 milligrammes of aluminium phosphate per millilitre. The method of their preparation has been described elsewhere (North and Patterson, 1953*a*). Group III received 0·5 millilitre of purified tetanus toxoid adsorbed onto aluminium phosphate (P.T.A.P.T.). It contained five Lf. of tetanus toxoid and 10 milligrammes of mineral carrier per millilitre. Group IV received one millilitre of crude formalinized tetanus toxoid (F.T.). This was the formalinized filtrate of *Clostridium tetani* cultures grown in peptone broth. It contained between two and five Lf. of tetanus toxoid per millilitre. Group V received one millilitre of purified tetanus toxoid (P.T.) in normal saline containing five Lf. of toxoid per millilitre. Group VI received one millilitre of purified tetanus toxoid (P.T.) in normal saline containing ten Lf. of toxoid per millilitre.

Seven and fourteen days after they had been injected with one or other of the foregoing antigens, blood was

again taken from the children. In a few cases no blood was obtained on the seventh or the fourteenth day.

The serum was assayed for tetanus antitoxin in mice against the reference Medical Research Council standard antitoxin or a local substandard serum at the $L_+/1000$ or $L_+/100$ level of dosage.

The levels of diphtheria antitoxin in the serum of children of groups I and II were also estimated by the intracutaneous method in guinea-pigs before as well as seven and fourteen days after the booster dose.

## Results.

Table I sets out the titres of tetanus antitoxin in the serum of all the children before, and seven and fourteen days after, the "booster" dose. In those cases in which insufficient serum was available to complete the assays, the geometric mean in a range is recorded. These titres, as well as those with a definite end-point, are in italics in the table. The other titres represent the least amount of tetanus antitoxin which was present.

Of 64 children whose serum was assayed, each had more than 0·01 unit and 75% had 0·1 unit or more of tetanus antitoxin per millilitre of serum six months after the primary course of immunization with C.D.T. Seven days after the "booster" dose 57 samples were assayed; every child had more than 0·1 unit per millilitre, two had 0·1 to 1·0 unit, 38 had 1·0 to 10·0 units, and 17 had over 10·0 units of tetanus antitoxin per millilitre of serum.

In groups I and II the mean "pre-booster" level of diphtheria antitoxin was 1·7 units per millilitre of serum, whilst seven and fourteen days after the "booster" dose the mean titres were 3·2 and 4·0 units per millilitre of serum respectively. These results were not further analysed.

### *Analysis of Tetanus Antitoxin Responses.*

As each group of children had received different treatments, it was necessary to know what variation in the level of serum antitoxin was present amongst the children before they received the "booster" dose. Only those titres which are in italics in Table I were considered. Analysis of variance of these titres showed that the variation between groups was not significantly different from the variation within groups six months after the earlier course of immunization (variance ratio, 1·3). Thus it was considered that the titres observed after the "booster" doses could be related to the effects of the different antigens which were used, despite the fact that there may be some correlation between initial titres and subsequent ones, as shown below.

In order to test the validity of the impression obtained from Table I, that the antibody response seven days after a "booster" dose of fluid toxoid was greater than that obtained after a similar interval with adsorbed toxoid, a table was constructed for comparing the results obtained after treatment with fluid and adsorbed toxoids. Only results from groups II, III, IV and V were used, because all these children had received approximately equal dosage of tetanus toxoid in the "booster" dose. The responses seven days after the "booster" dose were divided into those showing less than six units and those showing more than six units of tetanus antitoxin per millilitre of serum. Of 17 children who had received fluid toxoid, 15 had more and two had less than six units per millilitre of serum. On the other hand, of 23 children who had been injected with adsorbed toxoid, 18 had less and five had more than six units of tetanus antitoxin per millilitre of serum. By Fisher's (1948) test for independence in a 2 × 2 table, the probability of obtaining such a distribution by chance was 0·000034, a figure which confirmed the impression that, seven days after the "booster" dose, the rise in titre of tetanus antitoxin was higher after the use of fluid antigen than that obtained with the adsorbed product. By a similar analysis, titres obtained fourteen days after the "booster" dose also showed the superiority of fluid toxoid over the adsorbed product in producing a high antibody response ($P = 0·00055$). However, from the data

TABLE I.

*Tetanus Antitoxin Units per Millilitre of Serum just Prior to and Seven and Fourteen Days after a "Booster" Dose of Different Antigens Containing Tetanus Toxoid.*[1]

| Group. | Antigens. | Amount of Tetanus Toxoid per Injection (Lf.). | Titres of Tetanus Antitoxin. (Units per Millilitre of Serum.) | | |
|---|---|---|---|---|---|
| | | | Before "Booster" Dose. | At Seven Days. | At Fourteen Days. |
| I | Combined diphtheria and tetanus toxoid (C.D.T.). | 1·25 | 0·24 | 2·2 | 2·0 |
| | | | 0·24 | *6·4* | — |
| | | | 0·14 | *6·4* | *2·6* |
| | | | 0·14 | *1·2* | *1·4* |
| | | | 0·13 | 8·9 | *3·5* |
| | | | *0·13* | *4·5* | *3·5* |
| | | | 0·13 | *8·9* | *3·5* |
| | | | 0·13 | 2·2 | 3·7 |
| | | | *0·13* | *1·6* | *2·3* |
| | | | *0·13* | *2·4* | *4·6* |
| | | | *0·13* | 8·9 | *7·6* |
| | | | *0·12* | *2·2* | *2·3* |
| | | | *0·06* | *1·1* | *1·1* |
| Mean[2] | .. .. .. | — | 0·11 | 3·5 | 4·4 |
| II | Combined diphtheria and tetanus toxoid (C.D.T.). | 2·5 | 0·14 | *6·4* | 8·5 |
| | | | 0·14 | — | *5·2* |
| | | | 0·13 | *1·7* | *3·2* |
| | | | *0·13* | 3·2 | — |
| | | | *0·10* | — | — |
| | | | *0·10* | *4·8* | *4·7* |
| | | | *0·10* | *2·2* | *3·5* |
| | | | 0·10 | 8·9 | — |
| | | | *0·10* | *2·4* | *3·2* |
| | | | 0·10 | *2·4* | *5·2* |
| | | | *0·10* | — | *9·5* |
| | | | *0·08* | *1·1* | *2·0* |
| | | | *0·06* | *3·5* | *4·6* |
| | | | *0·02* | *0·6* | *1·2* |
| Mean[2] | .. .. .. | — | 0·09 | 2·8 | 4·2 |
| III | P.T.A.P.T. .. | 2·5 | 0·24 | *5·5* | 14·6 |
| | | | 0·24 | *14·6* | 14·6 |
| | | | 0·24 | *9·0* | 14·6 |
| | | | 0·14 | *4·4* | *9·0* |
| | | | 0·14 | — | 14·6 |
| | | | *0·13* | *1·3* | *5·0* |
| | | | *0·13* | *14·6* | 14·6 |
| | | | *0·09* | *5·0* | *8·1* |
| | | | *0·09* | *5·0* | *9·0* |
| | | | *0·08* | *4·4* | *5·0* |
| | | | *0·06* | *4·4* | *5·0* |
| | | | *0·05* | *4·4* | *8·1* |
| | | | *0·04* | *2·6* | *5·0* |
| | | | *0·01* | — | *2·6* |
| Mean[2] | .. .. .. | — | 0·07 | 6·3 | 6·0 |
| IV | Formalinised toxoid | 2·5 to 5·0 | 0·24 | 14·6 | 22·0 |
| | | | 0·24 | *12·8* | *9·7* |
| | | | *0·24* | *10·1* | *17·4* |
| | | | 0·14 | *17·4* | 14·0 |
| | | | 0·14 | 14·6 | *17·4* |
| | | | *0·13* | 14·6 | *13·8* |
| | | | 0·13 | 14·6 | 23·0 |
| | | | *0·13* | *23·0* | *17·4* |
| | | | *0·12* | *10·0* | 23·0 |
| | | | *0·09* | 14·6 | 23·0 |
| | | | *0·03* | *2·9* | *5·7* |
| Mean[2] | .. .. .. | | 0·12 | 12·7 | 14·8 |
| V | Purified liquid toxoid. | 5·0 | 0·14 | *8·0* | *12·0* |
| | | | 0·14 | *12·8* | *16·0* |
| | | | 0·13 | *16·0* | *16·0* |
| | | | 0·13 | *16·0* | *13·0* |
| | | | 0·13 | — | 18·0 |
| | | | *0·09* | *3·6* | *8·4* |
| | | | *0·05* | *8·0* | *13·0* |
| Mean[2] | .. .. .. | — | 0·07 | 10·7 | 12·7 |
| VI | Purified liquid toxoid. | 10·0 | 0·25 | *16·0* | *13·0* |
| | | | 0·24 | *16·0* | *16·0* |
| | | | *0·13* | — | *18·0* |
| | | | *0·13* | *16·0* | *13·0* |
| | | | *0·03* | *15·0* | *16·0* |
| Mean[2] | .. .. .. | — | 0·10 | 15·7 | 15·2 |

[1] When the titre is in italics, this indicates a definite end-point or the geometric mean of a range. All other titres are minimum titres.

[2] Calculated from titres which are in italics.

available at present, no inferences can be drawn regarding the comparative abilities of the different products to maintain high titres over a much longer period of time.

A comparison was made between the responses, after seven days, to the adsorbed product containing tetanus toxoid alone (P.T.A.P.T.) and those to the combined diphtheria and tetanus toxoids (C.D.T.). Application of the *t* test to the titres expressed as logarithms (Davis, 1949) showed that the titres obtained with C.D.T. as the "booster" dose were significantly smaller than those obtained with P.T.A.P.T. ($P < 0.05$). It thus appeared that the presence of diphtheria toxoid in the "booster" dose interfered with the antibody response to the tetanus component. Inspection of the individual titres of groups II and III obtained fourteen days after the booster dose (Table I) further supports the conclusion that interference did occur.

Analysis for correlation between "pre-booster" titres and those obtained seven days after the "booster" dose in groups I to IV showed a positive correlation approaching significance ($P = 0.07$). In other words, those with a high initial titre tended to give a somewhat higher antibody response to a booster dose of tetanus toxoid than did those with a lower initial titre.

It was of interest to know whether there was a significant rise in titre between the seventh and fourteenth days after the "booster" dose. Analysis of the antibody level of all the children's serum in which a definite end-point was obtained in both samples showed a significant rise between the seventh and fourteenth days after the "booster" dose in groups I to III ($P = 0.02$), whilst the rise found in groups IV to VI was not significant.

## Discussion.

Opinions differ as to what constitutes a protective level of tetanus antitoxin. The opinion most generally held is that after active immunization 0·01 to 0·1 unit of antitoxin per millilitre of serum will give protection against tetanus. All the children whose serum was examined six months after they had received two doses of combined diphtheria and tetanus toxoids had amounts of tetanus antitoxin in their serum which fell within or exceeded that range. Bigler (1951) has reported equally satisfactory levels of tetanus antitoxin in children who six months previously had received two doses of tetanus toxoid alone.

The maintenance of a protective level of circulating antitoxin is one of the objectives of active immunization against tetanus. The other and equally important purpose of active immunization against that disease is to induce a state of sensitization in the immunized person which will enable him to produce rapidly a high level of tetanus antitoxin after the administration of a "booster" dose of toxoid. The excellent antibody response obtained seven days after the "booster" injection in the present series of children showed that such sensitization had been accomplished. This was particularly well demonstrated in those children who had received only 1·25 Lf. of tetanus toxoid in the "booster" dose. In view of the observation (North and Patterson, 1953*b*) that basic immunization against tetanus can be satisfactorily carried out with two doses of adsorbed tetanus toxoid containing as little as 0·4 Lf. per millilitre, a "booster" dose containing an amount of tetanus toxoid considerably smaller than that which was used for the children of group I might be expected to have resulted in a satisfactory antibody response.

Although the response seven days after the "booster" dose containing tetanus toxoid adsorbed onto aluminium phosphate was highly satisfactory, that obtained with fluid toxoid was even better. Miller, Ryan and Beard (1949) reported that fluid toxoid, used for reinjection, induced a more rapid rise in antitoxin titre than alum-precipitated toxoid. Fluid toxoid would therefore appear preferable to the adsorbed product as a "wound booster" when an immunized subject suffers a wound liable to be infected with *Cl. tetani*.

From the present series no conclusions can be drawn concerning the comparative effectiveness of fluid and adsorbed toxoids in maintaining protective levels of tetanus antitoxin over a period longer than fourteen days. However, in view of the fact that basic immunization against tetanus can be carried out as effectively with two doses of adsorbed toxoid as with three doses of fluid toxoid (North and Patterson, 1953*b*), and in view of the more prolonged antigenic stimulus generally obtained with adsorbed toxoids, it is reasonable to suggest that adsorbed tetanus toxoid be the substance of choice for routine "booster" injections.

Barr and Jones (1953) have obtained results in guinea-pigs which suggest that interference with the antitoxin response to tetanus toxoid can occur in animals immunized with a combined prophylactic containing another antigen to which some immunity was already present. However, these authors did not expect this interference to occur after a "booster" dose containing both antigens if an immunity already existed to both its components.

The "booster" effect of adsorbed tetanus toxoid alone compared with that obtained after C.D.T. showed that the presence of diphtheria toxoid in the "booster" dose did interfere to some extent with the antibody response to the tetanus component. It is possible that this interference may be related to the preexisting immunity to diphtheria which was present in the children before this study was commenced. However, for confirmation further comparison of groups of children similarly treated but not possessing a preexisting immunity to diphtheria is required.

In the present series of children the over-all tetanus antitoxin response six months after the second injection of C.D.T. was adequate despite the presence of a preexisting immunity to diphtheria. In addition, the rapid and manifold increase of circulating antitoxin which occurred after a "booster" dose of tetanus toxoid indicated that adequate sensitization to tetanus toxoid had been induced in these cases. Although it is possible that the antibody response to tetanus toxoid six months after the second dose of C.D.T. might have been even better had there been no preexisting immunity to diphtheria, from a practical point of view, the administration of two doses of C.D.T. to children who had previously been immunized against diphtheria produced adequate sensitization to tetanus toxoid, as well as providing a protective titre of tetanus antitoxin for at least six months. In addition, reactions to C.D.T. were rare. (See Appendix.)

## Summary.

1. Six months after having received two doses of combined diphtheria and tetanus toxoids (C.D.T.) all of 64 children had a protective level of tetanus antitoxin in their serum (more than 0·01 unit per millilitre).

2. The antitoxin response within seven days after a "booster" dose of a prophylactic containing tetanus toxoid indicated that adequate sensitization had occurred in every subject.

3. A greater increase in the amount of circulating tetanus antitoxin followed the "booster" injection of fluid toxoid than was obtained with toxoid adsorbed on aluminium phosphate.

## Acknowledgements.

We are grateful to Dr. P. J. White and to Miss M. Campbell for technical assistance, and in particular to Mr. A. G. Mathews for assisting in the statistical analysis. We also wish to acknowledge the helpful advice given to us by Dr. E. A. North.

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### Appendix.

The children included in the foregoing report represented only a special section of a large number of children who were inoculated in an immunization campaign carried out in a rural municipality on the outskirts of Melbourne.

Nearly 1000 children aged between six months and fourteen years were injected with two doses, each of 0·5 millilitre of a combined diphtheria and tetanus prophylactic (C.D.T.), with an interval of six weeks between doses. A "booster" dose of 0·5 millilitre was given twelve months later. Prior to the primary course of immunization, about 60% of the children had received one or more injections of a diphtheria prophylactic.

Reactions were encountered in eight girls and four boys. All the 12 children who showed reactions were aged over seven years, and 10 of these had been previously immunized against diphtheria. Regardless of any previous history of immunization against diphtheria, no reactions were encountered in children aged under seven years.

Reactions included headache, abdominal pain and faintness. Some children developed swelling and excessive pain at the site of injection. Generalized urticaria developed in three children. In one case the skin over the site of inoculation broke down and a discharge occurred. As healing was rapid, the lesion was not believed to be an "alum abscess".

It is considered that C.D.T. is a safe prophylactic for the systematic control of tetanus in children.

The practical point in the use of tetanus toxoid concerns the attitude to be adopted by practitioners who are called upon to treat patients immunized against tetanus. In the present campaign, parents were informed by a circular letter that three injections against diphtheria and tetanus had been given to their children. All doctors in the district were notified that C.D.T. had been given, and that in these cases tetanus toxoid instead of tetanus antitoxin could be used in case of minor injury. There are, no doubt, shortcomings in this procedure. However, steps are being taken to provide parents with a complete record of all inoculations which their children have received. It is hoped that by this means the excessive and often unnecessary use of tetanus antitoxin, with the consequent risk of allergic reactions, will be reduced.

## "MYLERAN": A REVIEW OF ITS ACTION AND A REPORT ON ITS USE IN CHRONIC MYELOID LEUCHÆMIA.

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### Biological Action.

IN the past, useful palliation in chronic myeloid leuchæmia has been given by both irradiation and chemotherapy. The former may be used as deep X-ray therapy to the spleen or bone marrow, while total body irradiation has also had its vogue. Radioactive phosphorus provides an alternative to the last-named. Of these, irradiation of the spleen has probably been the most satisfactory, although the mechanisms involved are not really understood. Osgood (1951) has reported good results from the use of total body irradiation or radioactive phosphorus, both given at regular intervals without waiting for relapses.

Various forms of chemotherapy, such as benzol, arsenic, urethane and the mustards, including triethylene melamine, have been less reliable than splenic irradiation, owing to their toxicity and unpredictability, but nevertheless satisfactory results have frequently been obtained.

More recently added to the list of chemotherapeutic substances and elaborated by Timmis (Haddow and Timmis, 1953) is 1:4 dimethane-sulphonyloxybutane, known as G.T.41 or "Myleran", which has certain advantages over its predecessors, and can be compared more favourably with splenic irradiation as regards effectiveness and safety. It was developed as a result of work by Haddow, Kon and Ross (1948) on a series of aromatic analogues of nitrogen mustard, when efforts were made to improve on the usefulness of those substances. Timmis (Haddow and Timmis, 1953) synthesized certain sulphonic acid esters, the biological action of which was assumed to be similar to that of the nitrogen mustards, which meant that they could alkylate or take part in some chemical combination with a nucleophilic cellular constituent via their ethane or alkyl group.

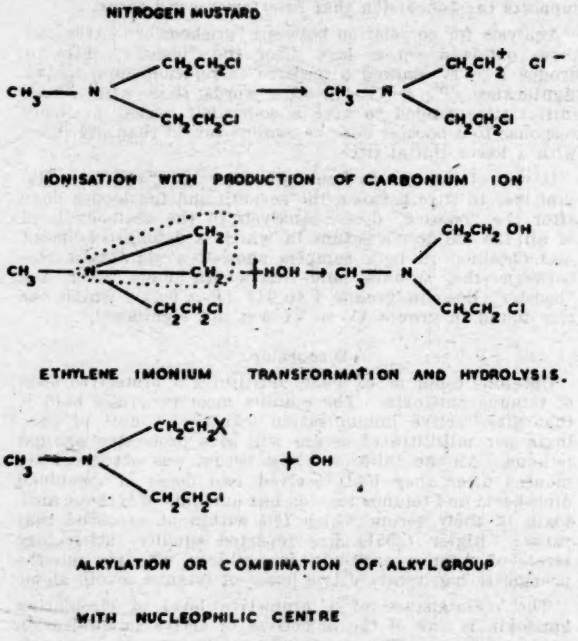



FIGURE I.

Thus in the case of nitrogen mustard (*Bis* compound) after ionization, carbonium ion formation with stabilization into the ethylene-imonium ion occurs. This is followed by hydrolysis, after which combination with the nucleophilic cellular centre takes place (Figure I).

Among the earlier sulphonic acid esters synthesized, one proved to be relatively less toxic to bone marrow than the nitrogen mustards, and it inhibited tumour growth in animals. This prompted further search and led to the selection by Timmis (Haddow and Timmis, 1953) of a series of compounds for investigation with the formula $CH_3SO_2O(CH_2)_NOSO_2CH_3$, where N may be from 2 to 10. This molecular structure of sulphonoxy groups, separated by methane groups capable of being varied by regular steps, allowed of a study of a series of resultant compounds with respect to their anti-neoplastic properties.

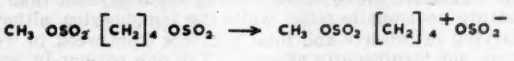
Optimum biological activity took place where N was 4 or 5; and when N was 4 (that is, with $CH_3SO_2O(CH_2)_4OSO_2CH_3$ or "Myleran"), marked granulocytic action occurred, suggesting its use in myeloid leuchæmia.

"Myleran" resembles the radiomimetic mustards, in that it is an alkylating cytotoxic drug causing chromosome breaks or mutations. It is also carcinogenic, and it reacts by the carbonium ion mechanism (Figure II).

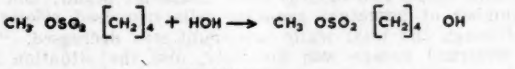
Formerly, it was thought that for these substances to react with nucleophilic centres, two alkylating groups were essential in their molecular structure, and that this resulted in the cross-linking of chromatids followed by chromosome

breaks at subsequent mitoses (Goldacre, Loveless and Ross, 1949).

It has since been shown, however, that molecules with only one such group are cytotoxic in the same way (Biesele *et alii*, 1950; Loveless and Ross, 1950); and because these possessed or produced in transformation unstable three-membered heterocyclic ring systems, as did substances like the nitrogen mustards and triethylene melamine, this factor was felt to be the significant one in their action. "Myleran", which has no such structure, negates this idea and also probably refutes the theory of Rose (1950), which



IONISATION AND CARBONIUM ION FORMATION



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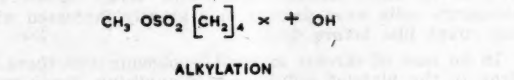

ALKYLATION

FIGURE II.

is that the group as a whole acts by the ability of its members to form linear polymers with reactive side chains, a property "Myleran" does not possess. It is probable, therefore, that more significance should be attached to the ability of these radiomimetic substances to react with nucleophilic centres by the carbonium ion mechanism (Loveless and Ross, 1950), even though possession of more than one reactive centre in the molecule does increase their action.

In the case of "Myleran", Timmis, as quoted by Haddow (1953), offers an alternative explanation when he says that its activity may be determined by its ability to form ring compounds with amino or sulphydryl groups, variations in activity being put down to the varying stability of the ring or its rate of formation.

The effects of "Myleran" and C.B.1348, an aromatic nitrogen mustard, have been compared, in experimental animals, on growth rate, blood and bone marrow (Elson, 1953). In the case of the mustard, a single dose caused severe initial weight loss; after recovery in the rat a second weight loss was infrequent, and, if the dose was toxic, death occurred mostly during the first weight loss.

There was a rapid fall in the number of circulating lymphocytes and neutrophile cells, followed by a marked neutrophilia, which reached its peak in eight to ten days.

The number of neutrophile cells returned to normal fairly quickly after treatment with the mustard and usually did not fall again. The number of lymphocytes, after initial depression, returned to normal in fifteen to twenty days. The hæmoglobin value rose somewhat in the initial weight loss period, and then fell slightly to a minimum at about the time of the maximum degree of neutrophilia. There was no rapid fall except in the few cases in which a second weight loss occurred. "Myleran", on the other hand, after a single dose caused only a very slight initial weight loss in the rat; and if death occurred as the result of a toxic dose, it did so during a second weight loss period and was due to massive hæmorrhage. There was no effect on the circulating lymphocytes, the main effect being a steady fall in the number of neutrophile cells, so that these reached their minimum about twelve days after treatment. There was also a marked fall in the number of platelets; and, as in the case of X irradiation, the hæmorrhagic state was probably brought about by deprivation of platelets, and the second weight loss followed anæmia due to the hæmorrhage.

From this work it seemed that the effects of X rays on lymphoid tissue were reproduced by the nitrogen mustards, and their effects on myeloid tissue by "Myleran".

It was reasonable to suppose that a complete radiomimetic effect could be obtained if the two were combined, and this was done, equal amounts being used of more than half the lethal dose of each. After this dual therapy, no animal succumbed, which demonstrated that their effects were not additive, and that they acted in an independent manner. The nitrogen mustard element was probably almost entirely responsible for an initial weight loss which took place, and the combined therapy probably brought about in the blood picture a flattening of the peak in the neutrophile cell curve caused by the neutrophilia at eight days due to the mustard. Bone marrow studies were proceeding; but, according to Elson, blood and growth changes, very similar to those following exposure to a single dose of whole body X irradiation, occurred as a general effect, after combined therapy as above. This similarity was so close that ideas on the effects of X irradiation may have to be reconsidered—namely, whether these are not the result of chemical changes of two distinct types, which occur simultaneously.

This is more interesting when it is known that the mustards act by what is called an $SN_1$ type of reaction and "Myleran" by an $SN_2$ mechanism, in reactions involving these cytotoxic alkylating agents. In the first instance, the rate of reaction by the reagent depends on its rate of ionization, which depends in turn on the medium and not on the nature and concentration of the groups in the body cells with which the reaction takes place. With the $SN_2$ mechanism, high concentrations of cellular constituents with which a compound reacts are essential, and, unless the two systems approach each other, no combination takes place. It follows that where cells of any tissue contain a high concentration of groups capable of reacting, an increased amount of the introduced substance will be involved.

It seems that moderate dosage of "Myleran" may act by holding up cell division in bone marrow, but that more cell destruction may be caused by the nitrogen mustards.

### Clinical Use.

Following the work of Timmis and Haddow, Galton (1953) reported the clinical use of "Myleran" given orally in 19 cases. Seven of the patients had had no previous treatment, while the remainder had been treated by other methods, which included splenic irradiation.

Galton noted symptomatic relief, improvement in hæmoglobin value and splenic regression, while granulopenia occurred in all cases, the rate depending on the dosage schedule used.

The immature myeloid cells were affected to a greater degree than were the mature neutrophile cells, while the effect on the lymphocytes was inconstant. Some diffuse brownish facial pigmentation and thrombocytopenia were the only side actions noted, although the number of platelets fell in all patients, the degree depending on the dosage. Resistance occurred in repeat courses in certain patients.

One dosage schedule was to give four to 10 milligrammes daily for four to sixteen weeks to a total of 200 to 500 milligrammes; another was to administer 100 to 150 milligrammes in short courses of one to six days.

Attempts at maintenance therapy were made, four to six milligrammes being given daily. In a later report by Galton and Till (1953) maintenance doses as low as two milligrammes daily were given with success. Galton felt that "Myleran" was generally superior to other drugs in its results, and had the further advantages of ease of administration and lack of side effects. He did not regard it as being superior to X-ray therapy, but regarded it as having certain advantages, such as not causing radiation sickness. It did not have the disadvantage of requiring special centres for its use, and perisplenitis with decreasing splenic regression after X-ray therapy did not occur. Its use was considered warranted in cases in which radio-

therapy would normally be given, and in cases in which the latter had ceased to be of use. Petrakis *et alii* (1954), reporting on 21 cases, confirmed Galton's work and, like him, found no benefit in cases of acute myeloid or monocytic leuchæmia. Most of their patients had had previous treatment with X-ray therapy, and their dosage schedule differed somewhat. In some cases the drug was given intravenously in doses ranging from 10 to 60 milligrammes. The side effects noted were the same. The results of the oral treatment with "Myleran" of 13 patients (10 females and three males) are reported in the present paper, and the kindness of Dr. D. A. G. Galton in forwarding the early supplies of the drug is appreciated.

The first patient's treatment began on October 5, 1953, and the cases included 10 of chronic myeloid leuchæmia, one of aleuchæmic myeloid leuchæmia, and two of monocytic leuchæmia of the mixed type.

Seven of the patients with chronic myeloid leuchæmia responded well initially, and five of these remain alive and well. Of the other three, one was *in extremis* when administration of the drug was commenced, one died from hæmorrhage following *paracentesis abdominis* shortly after "Myleran" treatment was begun, while the third did not cooperate fully in his treatment and, similarly, soon after its inception, died in a country hospital.

One of the seven patients who responded died after continuous treatment for nine months, during the greater part of which time she felt well, and one died from another cause, with the leuchæmia controlled, forty-eight weeks after treatment was begun. The other five are still being treated, and their condition is satisfactory as regards their leuchæmia.

The response was unsatisfactory in both cases of monocytic leuchæmia, although from time to time immature granular cells appeared in significant numbers in the peripheral blood. In one case, there was a profound diminution of hæmoglobin and white cell values during treatment, and an even greater diminution in the number of platelets; while in the other case there was very little change in the white cell count, although for a time reasonable health was maintained on a reduced hæmoglobin level, and the percentage of immature granular cells in the peripheral blood decreased.

The result in the first case suggested marrow hypoplasia rather than any direct effect by "Myleran". In the second, a spontaneous remission could have been responsible. The response was poor in the case of aleuchæmic myeloid leuchæmia.

The dosage scheme adopted was that of a low daily dosage on a long-term continuous basis, with variations from time to time as the blood count altered. It was found necessary in certain cases to cease the treatment for varying periods; but, if it was resumed, the low dosage schedule was again adopted. The patients were encouraged to regard their disease as being in the same category as pernicious anæmia or diabetes, for which continuous observation and laboratory control are necessary.

Bone marrow examinations were made, where possible, before treatment and when it was felt that a reasonable period of control had been obtained, but the fact that several of the patients lived in the country and found it difficult always to attend when required made this examination awkward to arrange at times.

None of the seven patients who responded required transfusions in combination with the "Myleran", and all of them had responded to their last course of X-ray therapy.

In one, the spleen was not palpable at the commencement of "Myleran" therapy, having diminished considerably in size after previous irradiation. No change was noted after "Myleran" was given.

In two patients there was no significant change in the spleen after "Myleran", although it was moderately enlarged in each case. Diminution in splenic size had occurred in each case as the result of the previous X-ray therapy course.

In three patients the spleen became impalpable or much decreased, the response in each case being better than with the previous therapy course. The patient who died after being controlled for nine months was in this group, but her spleen enlarged rapidly in the terminal phases, despite increase in "Myleran" dosage. The remaining patient in this group had a very rapid recession of her splenic tumour with irradiation, the response with "Myleran" being similar, but slightly slower.

In two of the patients of the group no significant change in hæmoglobin value occurred, while in five there was an increase. In six cases the total white cell count decreased, the immature granular cells being more affected than the mature neutrophile cells; while the lymphocytes, although varying in relative and total numbers from week to week, were not significantly affected. The one patient in whom the immature granular cells did not respond in this way had an attack of pyrexia, associated with a drop in hæmoglobin value, two months after treatment began; and the number of immature granular cells increased relatively, although the total white cell count was decreased. The "Myleran" dosage was increased, and the situation has slowly improved, but there are still appreciable numbers of immature granular cells present. In the patient who died after nine months' treatment, large numbers of immature cells were present in a greatly increased white cell count just before death.

In no case of chronic myeloid leuchæmia was there any drop in the platelet count, and, if anything, there was a tendency for an increase in numbers and the production of giant forms. This occurred even when bone marrow cellularity had decreased, and in one case there were 950,000 platelets per cubic millimetre present in the blood.

The bone marrow examinations carried out showed that the peripheral blood changes were preceded by similar changes in the marrow. Cellularity was not always decreased, but the myeloid-erythroid ratio was in most instances much reduced. There was no significant decrease in the number of megakaryocytes, and in some examinations they were increased in numbers and size.

As all the patients who responded favourably to "Myleran" had been previously treated by and had improved after splenic irradiation, it was possible within certain limits to compare the rapidity of the response in each case and, more accurately, the periods of control obtained.

With "Myleran", all who improved were treated as outpatients from the first; but as some lived long distances away, so blood counts, marrow examinations and splenic measurements could not be carried out as frequently as desired, although great help was given by local doctors in this respect.

In comparing the effects of the drug with irradiation, blood counts and splenic measurements previously necessary to control and assess X-ray therapy were used, but these had not been consistently recorded.

Within these limitations, however, the impression gained was that there was no significant difference in the rate of response in the case of the white cell count and hæmoglobin value. As far as splenic regression was concerned, the one patient who responded to both forms of treatment did so slightly more rapidly in the case of irradiation. Two patients reacted to splenic irradiation and not to "Myleran", and three reacted in the reverse manner, but those who responded to X-ray therapy did not do so at a significantly different rate from those who improved on "Myleran".

In assessing the value of treatment, the term "period of control" rather than remission has been used; and in the use of "Myleran" the disease was considered to be under control if a decreasing hæmoglobin value and increasing white cell count (even up to 50,000 per cubic millimetre) could be controlled by an increase in "Myleran" dosage, and if at the same time the patient felt well and had no increase in splenic size.

## Reports of Cases.

CASE I.—This case is represented graphically in Figure III. The patient, a young married woman, aged thirty-two years, complained of tiredness and metrorrhagia for the four months prior to first being examined, and had noticed bruises on her legs for the previous month. She was found to have an enlarged spleen. The peripheral blood findings were as follows: hæmoglobin value, 75% or 11·1 grammes per 100 cubic centimetres (100% = 14·8 grammes per 100 cubic centimetres); total erythrocyte count, 3,800,000 per cubic millimetre; total leucocyte count, 120,000 per cubic millimetre

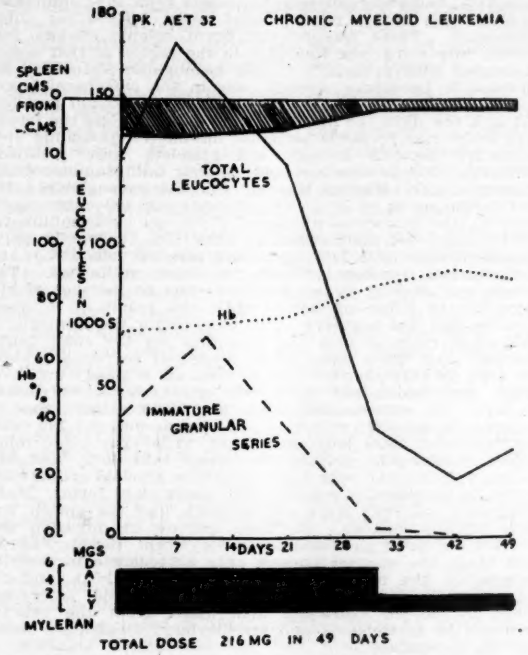


FIGURE III.

(including neutrophile polymorphonuclear cells 33% and immature myeloid cells 55%); total platelet count 390,000 per cubic millimetre. Peripheral gland and bone marrow biopsy confirmed the diagnosis of chronic myeloid leuchæmia; so the spleen was irradiated and a remission of five months resulted. The chief effect was on the leucocyte count and hæmoglobin value; the splenic reaction was not marked. The uterus was removed during this period for metrorrhagia. The remission ended when the blood picture was found to be as follows: hæmoglobin value, 69% (10·2 grammes per 100 cubic centimetres); total leucocyte count, 139,000 per cubic millimetre (including neutrophile polymorphonuclear cells 68% and immature myeloid cells 23%); platelets, plentiful. The spleen was palpable 6·5 centimetres below the costal margin; it was given two very small doses of X-ray therapy and then "Myleran", six milligrammes daily, was substituted. The leucocyte count, which rose at first, was a month later 35,850 per cubic millimetre (including neutrophile polymorphonuclear cells 72% and immature myeloid cells 7%) with a hæmoglobin level of 86% (12·8 grammes per 100 cubic centimetres). The spleen was much smaller and the patient felt better, except for a low backache, the cause of which was never discovered despite investigation. "Myleran" dosage was reduced, and from then on was varied according to the blood count. The spleen became impalpable and the white cell count was maintained between 10,000 and 50,000 per cubic millimetre until nine months after commencement of treatment. The spleen then began to enlarge rapidly and became painful, while hæmorrhages appeared on the legs. Despite increased "Myleran" dosage, the white cell count rose, the immature myeloid cells becoming more plentiful. Administration of "Myleran" was ceased, as the patient was vomiting frequently, and at this stage the white cell count was 105,000 per cubic millimetre, of which 81% were immature forms (63% myeloblasts). The spleen was palpable seven centimetres below the left costal margin, but bruising had ceased, platelets being plentiful, though abnormally large and vacuolated. Blood transfusion was given and another course of deep X-ray therapy commenced, but the patient died ten months after the "Myleran" treatment had commenced.

**This patient became resistant to "Myleran"; but although it was never possible to cease treatment, her condition had been controlled for nine months without side effects. The terminal nausea and vomiting were probably due to her general condition rather than to the drug.**

CASE II.—This case is represented graphically in Figure IV. The patient, a young married woman of thirty years, complained of increasing weakness and tiredness for the previous two years. She had been confined two months previously and had had a severe post-partum hæmorrhage. She was pale, with a grossly enlarged spleen, and a blood count gave the following findings: hæmoglobin value 72% (10·6 grammes per 100 cubic centimetres); total leucocyte count, 110,000 per cubic millimetre (including neutrophile cells 53% and immature myeloid cells 42%); total reticulocyte count, 1%; platelets, very numerous. The picture was that of chronic myeloid leuchæmia, and X-ray therapy to the spleen was begun. The white cell count decreased, but a drop also occurred in the hæmoglobin level and platelets, while the spleen, if anything, increased slightly in size. Transfusions were necessary before and after X-ray therapy was ceased, but despite a subsequent drop of hæmoglobin level to 67%

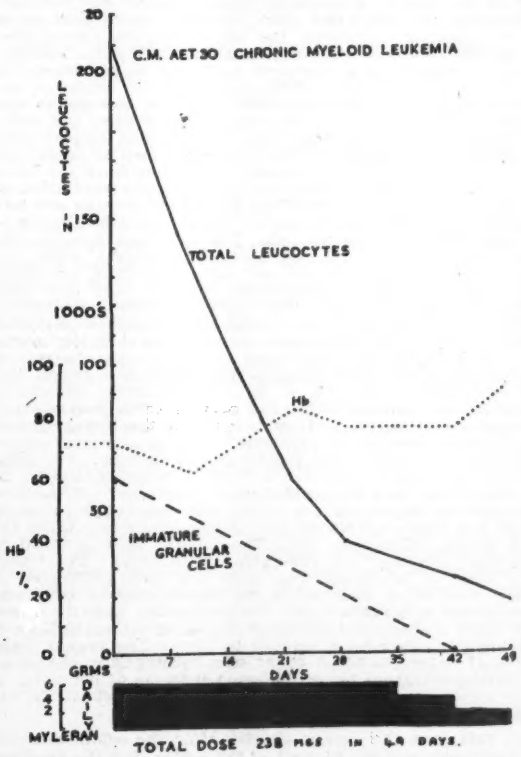


FIGURE IV.

(9·9 grammes per 100 cubic centimetres) and of the leucocyte count to 1800 per cubic millimetre, the patient gradually improved; and two months after finishing treatment the hæmoglobin value was 85% (12·6 grammes per 100 cubic centimetres) and the leucocyte count was 13,600 per cubic millimetre. Seven months later the patient suffered a relapse; the hæmoglobin estimation was 65% (9·6 grammes per 100 cubic centimetres), while the white cell count was 250,000 per cubic millimetre, of which 55% were neutrophile polymorphonuclear cells and 32% immature myeloid cells. Platelets were plentiful, and a bone marrow smear was characteristic of chronic myeloid leuchæmia with myeloblasts in normal proportion. The myeloid-erythroid ratio was 24:1.

A course of "Myleran" was commenced, and with a dosage of six milligrammes daily the response was satisfactory in that, one month later, the hæmoglobin value was 76% (11·3 grammes per 100 cubic centimetres) and the leucocyte count 24,600 per cubic millimetre, of which 77% were neutrophile polymorphonuclear cells and only 5% immature myeloid cells. The spleen was impalpable. Four months after its commencement "Myleran" therapy was ceased, as the white cell count was 8,250 per cubic millimetre, with no immature forms present, while the hæmoglobin value was 94% (13·9 grammes per 100 cubic centimetres). Since then the patient has remained well without splenic enlargement, the results of blood examination nine months after "Myleran" therapy being as follows: hæmoglobin value, 88% (13 grammes per 100 cubic centimetres); total erythrocyte count, 4,300,000 per cubic millimetre; total leucocyte count, 14,050 per cubic millimetre (including neutrophile polymorphonuclear cells 61% and immature myeloid cells 20%).

**This patient's response to "Myleran" therapy was very satisfactory; and although low dosage was used throughout, it was ultimately possible to cease treatment, in contrast to Case I, in which the patient was never able to do without the drug on the dosage scale used.**

CASE III.—A married woman of forty-seven years had complained of pain in the left side and fever for some weeks prior to being examined on September 28, 1951, when she was found to have an enlarged liver and spleen. Hæmatological investigation established a diagnosis of chronic myeloid leuchæmia. A course of X-ray therapy was effective in reducing the white cell count, but the hæmoglobin value did not improve, although the spleen became impalpable. No further treatment was required for over twelve months, when she was given a course of urethane, as the leucocyte count was rising again. This controlled the condition for three months, but another course of X-ray therapy to the spleen became necessary. The immediate response was good, but relapse some months afterwards was again treated with urethane. A few months later this again lost its effect and the bone marrow and blood examinations confirmed the state of relapse. The immediate response to a third irradiation of the spleen was good, but in less than four months she felt ill again, and both spleen and liver were palpable six centimetres below the costal margin. The hæmoglobin value was 105% (15·6 grammes per 100 cubic centimetres), while the leucocyte count was 110,000 per cubic millimetre, of which 49% were neutrophile polymorphonuclear cells and 39% immature myeloid cells. The platelets were increased in number. A bone marrow examination showed increased cellularity in a general picture of chronic myeloid leuchæmia with a myeloid-erythroid ratio of 50:1. A course of "Myleran" therapy (six milligrammes daily) was begun, but the leucocyte count rose to 295,000 per cubic millimetre, while the hæmoglobin value fell to 85% (12·6 grammes per 100 cubic centimetres). It was felt that the patient might prove to be resistant to "Myleran", and arrangements were made to admit her to hospital for X-ray therapy. She went back to the country before this could be done, continuing in the meantime on a higher dosage of "Myleran". When she returned to Melbourne the white cell count had fallen to 52,500 per cubic millimetre, and continued to fall, while the hæmoglobin value rose, until two months later it stood at 98% (14·5 grammes per 100 cubic centimetres). The leucocyte count at this stage was 22,400 per cubic millimetre, of which 66% were neutrophile polymorphonuclear cells and 11% immature myeloid cells. The patient felt well, the spleen was much smaller and the liver was impalpable, the dose of "Myleran" having been reduced to four milligrammes daily. A month later the blood count was substantially the same, a continued feature being the great increase of platelets. A bone marrow examination showed still much cellularity, but a decrease in myeloid-erythroid ratio to 13:1.

**In this case, the dosage shortly after the commencement of treatment was the highest of the series, and the response was striking.**

CASE IV.—A married woman of thirty-seven years, in the thirty-three months prior to commencing treatment with "Myleran", had had four courses of splenic irradiation for chronic myeloid leuchæmia. These produced remissions of fourteen, nine, four and three months respectively. Blood transfusion was necessary after the first of these, as the erythrocyte and platelet counts were low, and also during the second, owing to a low platelet count. Hypersplenism was suspected and splenectomy considered, but irradiation of the spleen was preferred at that stage. The splenic tumour disappeared after each course of therapy. At the end of the last remission she reported feeling very ill, with pyrexia, joint pains and bruises. The spleen was palpable seven centimetres below the costal margin, and the blood examination showed a hæmoglobin value of 70% (10·4 grammes per 100 cubic centimetres), a total leucocyte count of 46,000 per cubic millimetre (including neutrophile polymorphonuclear cells 73% and immature myeloid cells 25%). Administration of "Myleran" (six milligrammes daily) was begun, and the general symptoms were quickly relieved. At first the leucocytes increased in number to 70,000 per cubic millimetre (including myeloid cells 43%), and the platelet count also rose; but the hæmoglobin value decreased slowly for the first month, by which time "Myleran" dosage had been reduced to two milligrammes daily. A month later the blood findings were as follows: hæmoglobin value, 76% (11·3 grammes per 100 cubic centimetres); total leucocyte count, 23,000 per cubic millimetre (neutrophile polymorphonuclear cells 55%, basophile polymorphonuclear cells 16%, immature myeloid cells 28%); total platelet count 340,000 per cubic millimetre. There was no significant splenic change, but shortly afterwards she had pain in the region of that organ associated with pyrexia, a falling hæmoglobin value and an increase in immature myeloid cells in the peripheral blood. A splenic infarction with hypersplenism was thought possible, but in a few days the hæmoglobin improved, while the leucocyte count rose to 64,000 per cubic millimetre (including 31% immature myeloid series), and platelets were plentiful. "Myleran" dosage was increased to four milligrammes daily. A month later, although she felt well, the hæmoglobin value had fallen again to 59% (8·8 grammes per 100 cubic centimetres), the leucocytes numbered 27,700 per cubic millimetre (neutrophile polymorphonuclear cells 59%, basophile polymorphonuclear cells 29%, immature myeloid cells 10%), and the platelets numbered 250,000 per cubic millimetre. The spleen was slightly larger, but there was no increase of bile pigments in urine or fæces, while the result of a direct Coombs test was negative. Two weeks later the hæmoglobin value had risen to 65% (9·6 grammes per 100 cubic centimetres), and there were many nucleated red cells present with 7% of reticulocytes. From then on, a steady improvement was maintained until ten months after "Myleran" therapy was commenced, when the blood picture was as follows: hæmoglobin value, 84% (12·4 grammes per 100 cubic centimetres); total leucocyte count, 12,200 per cubic millimetre (neutrophile polymorphonuclear cells 40%, basophile polymorphonuclear cells 45%, immature myeloid cells 12%); platelets, increased in number with many giant forms. Many nucleated red cells were still present, and the spleen was only slightly smaller. No bone marrow examination was carried out prior to commencing "Myleran" therapy, but at this stage the marrow showed only a moderate increase in cellularity, the myeloid-erythroid ratio was 1·5:1, and the pathologist's comment was that the myeloid leuchæmic element was in remission and, apart from the relative increase in myeloblasts and myelocytes, its existence would not be recognized.

**Splenectomy may still be indicated for this patient, to correct a secondary hypersplenism, although further irradiation of the organ could be tried. The value of the latter alone is doubtful, as the last course did not produce any great increase in hæmoglobin value and was responsible for only short remissions on the last two occasions on which it was used. It is possible that low dose X-ray courses used concurrently with "Myleran" may be of value. "Myleran", of course, could have caused red cell hæmolysis, but the question of hypersplenism had been considered in this patient long before it was used. On the whole, it has controlled the leuchæmia without abolishing the immature white cells, but the responses of the hæmoglobin and splenic tumour have been disappointing, especially as the spleen may be playing an important role in hæmolysing red cells in this case. For the most part, the patient has felt well while taking the drug and has managed without transfusions, and the period of control has been almost four times that of the last X-ray therapy course.**

### Discussion.

**The results obtained in the present series of cases bear out the observation of Galton and Petrakis that "Myleran" is effective in the treatment of chronic myeloid leuchæmia. The same lack of side effects is noted, and it seems that continuous dosage is well tolerated. It has, therefore, definite advantages over urethane and triethylene melamine, but its value relative to X-ray therapy is harder to assess in this series. It was effective in seven of the cases in which X-ray therapy had been successful previously, and when ineffective was probably so because of the terminal phase of the illness rather than its own demerits.**

**The average period of control achieved by the last X-ray therapy course prior to commencing treatment with the**

drug, in patients responsive to both, was nineteen weeks. If irradiation had been used again, it seems likely from past experience that this period would have been shorter rather than longer, and would continue to decrease with successive treatments; therefore, the average control period of thirty-seven weeks achieved with "Myleran" in the same group appears to be an improvement. The possibility, however, of producing a similar period of good health with the use of further courses of irradiation instead of "Myleran" cannot be entirely ruled out, and it seems that the only reasonable way of closely comparing the two methods is to measure the total control periods gained with each. This should be done by noting the effect of intermittent courses of "Myleran" and X-ray therapy on similar untreated subjects, or comparing the results of continuous "Myleran" dosage with methods such as Osgood's.

However, X-ray therapy requires special centres for its use, and may cause irradiation sickness, although this was not marked in the present series. The necessity for hæmatological checks is as great or possibly greater with "Myleran"; so the patient is not absolved from frequent attendances, especially in the early stages, and even after reasonable control these should be at least monthly.

No previously untreated patients were given "Myleran" as the first therapy, so its effect compared with radiotherapy as the initial treatment could not be assessed; but its effect in relapses was largely satisfactory, so it is reasonable to assume that it would not be inferior to irradiation in previously untreated subjects. It seems, therefore, that "Myleran" can compare favourably with splenic irradiation in the treatment of chronic myeloid leuchæmia and, as Galton suggests, may succeed where irradiation fails, although the reverse is also possible.

There may be a field for the two methods used alternately, and even a place for their concurrent use (for example, Case IV).

X-ray therapy to the spleen, while a most convenient method, may not be the most effective form of radiotherapy in this disease, and Osgood's (1951) method deserves further consideration.

The value of any form of treatment in chronic myeloid leuchæmia should be viewed in the light of the fact that the actual extension of life expectancy given by any method is probably small, and the fact that success is better judged by the proportion of normal life in the total course of his disease that a patient can enjoy. "Myleran" probably succeeds as well as most other treatments in this respect, but any method involving frequent attendances and investigations must cause much anxiety to those treated, even if they feel bodily well. It therefore still leaves much to be desired as a treatment *per se*, but may point the way to further improvements.

It seems to be of undoubted value for patients living long distances from large centres.

### Acknowledgements.

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## THE SIGNIFICANCE AND MANAGEMENT OF MECONIUM IN THE LIQUOR AMNII DURING LABOUR.

By V. T. WHITE, M.B., B.S. (Melbourne), M.R.C.O.G., *Perth*.

DURING the last three decades there has been such a decrease in maternal mortality that now maternal death usually results only from an "accident" of childbirth. Particularly since the widespread use of the lower segment Cæsarean section, blood transfusion, chemotherapy and antibiotics has this increased safety been reflected in the much lower mortality of operative obstetrics. Unfortunately, although some progress is apparent, there has not been so great a fall in fœtal and neonatal mortality.

More and more interest has therefore been taken in the fate of the fœtus, and few will argue against the occasional validity of purely fœtal indications for operative interference, including Cæsarean section.

Most text-books list meconium staining as a sign of fœtal distress, but do not indicate whether, or when, its occurrence will warrant interference. The decision to interfere is particularly hard to make when the meconium is seen during the first stage of labour, and before deciding to perform Cæsarean section one should always remember the following facts: (i) "The maternal mortality of Cæsarean section is 0·5%" (Drew-Smythe, 1950). (ii) "The fœtal mortality in the series of Cæsarean sections was 11·6%—in few series is the figure below 5%, and in many it is over 10%" (Williams, 1950).

### Material for Discussion.

An analysis of 4350 consecutive deliveries at the Marston Green Maternity Hospital, Birmingham, has been made in an attempt to throw some light on the significance of the finding of meconium staining of the liquor.

Of the 4350 deliveries, meconium staining was noted in 217 in which the head was presenting, an incidence of 5%. This compares with an incidence of 3% found by Schultze (1925).

Necessity to resuscitate the infant after delivery was taken as the only criterion of fœtal distress, and resuscitation was taken to mean any measures, in addition to clearing the airways, required to initiate respiration.

Of the infants with meconium staining, 72 required resuscitation, an incidence of 33% compared with an

incidence of 7·5% among infants without meconium staining. The much higher rate of forceps deliveries and Cæsarean section in the meconium-stained group may be a possible causative factor in this substantial difference. There were 37 forceps deliveries (17%), and 23 infants required resuscitation; there were 12 Cæsarean sections (5·5%), and eight infants required resuscitation.

If the operative deliveries are completely excluded, then the incidence of resuscitation is 24·4%, which is still quite a significant difference. However, most of the operative procedures were undertaken only when there were additional signs of fœtal distress.

It would seem, therefore, that the occurrence of meconium staining does mean that there is more, although by no means absolute, likelihood of fœtal distress at delivery. Other signs must be sought to help determine what is happening to the fœtus.

### Causes and Significance.

Brews (1948) states that the increased fœtal peristalsis which accompanies the early stages of asphyxia is the cause of meconium staining. Certainly this contention is often supported at the post-mortem examination, when the bowel of a fœtus that has died an asphyxial death can almost always be seen emptied of meconium and frequently in obvious spasm.

Another possible mechanism is relaxation of the anal sphincter due to severe anoxia allowing escape of the meconium (Reed, 1918).

There is little doubt that either or both of these factors can be a cause; but they are not necessarily the only causes, for it would seem that the appearance of meconium in a vertex presentation is sometimes not associated with detectable fœtal anoxia. However, Walker (1954) categorically states that "when meconium is passed, the saturation of the blood in the umbilical vein is at or below 30%, and the fœtus is not obtaining enough oxygen to survive indefinitely".

### *Significance of Colour.*

1. Golden yellow. Clifford (1948) associates a golden yellow colour with the placental insufficiency syndrome, and regards it as being indicative of placental disease causing transient anoxia some time prior to the commencement of labour. Two such cases have been encountered. It must be remembered, however, that golden liquor may also be seen in association with rhesus incompatibility.

2. Uniform olive green. This appears on rupture of the membranes, whether this occurs before or during labour, and Greenhill (1947a) regards it as being due to the passage of meconium some time previous to its appearance.

3. Olive green with flakes of meconium. It would seem logical to regard this as of more recent origin than type 2.

There were 117 cases of types 2 and 3 combined, and 25·6% of the infants required resuscitation.

4. Black to sea-green. *This indicates fresh meconium* appearing during labour; frequently almost pure meconium appears to be draining away, with very little admixture of liquor.

Fresh meconium was observed 100 times, and 42% of the infants required resuscitation. It would therefore seem that fresh meconium is of much more significance than the older staining.

### Ætiology and Diagnosis of Anoxia.

On the whole it appears that the presence of meconium in the liquor, whether fresh or old, should be regarded as a sign of fœtal anoxia, and a cause should be assiduously sought.

### *Ætiology.*

Clemetson (1953) classifies the causes of fœtal anoxia as follows: (i) anoxæmic anoxia, (ii) anæmic anoxia, (iii) cord obstruction anoxia, (iv) histotoxic anoxia, (v) anoxia due to other factors.

*Anoxæmic Anoxia.*—Anoxæmic anoxia may be due to retroplacental hæmorrhage, maternal anoxia, severe maternal anæmia, a drop in maternal blood pressure or some factor connected with Cæsarean section. With perhaps the exception of retroplacental clot, all these factors can readily be checked, and even the presence of retroplacental clot usually declares itself before very long.

*Anæmic Anoxia.*—Anæmic anoxia may be due to erythroblastosis or to fœtal hæmorrhage. The possibility of the former is usually known prior to labour, and the latter, besides being very rare, usually proclaims itself by a brisk ante-partum hæmorrhage.

*Cord Obstruction Anoxia.*—Factors producing cord obstruction anoxia are as follows: (i) cord around the fœtus, (ii) prolapse of the cord, (iii) a true knot in the cord, (iv) breech delivery, or (v) a short cord. Apart from such rare cases as that described by Gardiner (1934), prolapse of the cord is the only one of these complications that one is likely to diagnose prior to delivery. This can almost always be done by vaginal examination. The work of Clemetson and Churchman (1953) emphasizes the importance of lesser degrees of cord involvement as a cause of fœtal anoxia.

*Histotoxic Anoxia.*—Histotoxic anoxia is due to narcotics. On the whole this type is regarded too lightly, and the statement by Gibson and McGarney (1950) that "fœtal narcosis, anoxia and subsequent death occur too frequently from the ill-advised administration of analgesics, hypnotics and sedatives" contains more truth than is generally recognized.

*Other Factors.*—Other factors likely to produce fœtal anoxia are as follows: (i) vascular anastomosis of homozygous twins, (ii) post-maturity, (iii) placental insufficiency, (iv) uterine hypertonus, (v) uterine retraction, (vi) *placenta prævia*, (vii) placental infarction, (viii) preeclampsia. This group includes a number of important factors which I would put together as "decreased placental reserve" under the heading of anoxæmic anoxia. Prolonged labour, especially if the mother's pelvis is small, should also be mentioned.

### *Diagnosis of Anoxia.*

From the facts so far presented it would seem that meconium staining *per se* is not a definite sign of fœtal anoxia. What, then, are the other signs of value?

Most text-books list the signs of fœtal distress as follows: (i) a fœtal heart rate less than 110 per minute, (ii) a fœtal heart rate more than 160 per minute, (iii) irregularity of rhythm of the fœtal heart, (iv) meconium staining of the liquor, (v) convulsive fœtal movements.

On the last-mentioned sign, Lund (1943*a*) fairly remarks: "Excessive fœtal movements are at best an elusive, if not a delusive sign." It is usually agonal and little can be done to save the fœtus.

Changes in fœtal heart rate and rhythm then are left as possible indications of fœtal anoxia.

Lund (1943*b*) quotes Von Winchel, writing in 1903, as being the first to state that a fœtal heart rate below 110 or above 160 per minute is indicative of fœtal distress. He further states that in 1917 Baumm upheld this latter observation as an indication of fœtal distress.

Since then, however, the majority of writers have come to the conclusion that a fœtal heart rate dropping to 100 or even 110 per minute is the most reliable indication of fœtal anoxia, and that a fœtal heart rate raised above 160 per minute is both rare and of little significance.

It is usually agreed that the vagal release which is the cause of the rapid heart rate during the early stages of anoxia in the adult does not occur in the fœtus or the neonate. Increased fœtal heart rate is more likely to result from fœtal movement or raised maternal temperature. Bartholomew (1925), Freed (1927) and Lund (1943*b*) all support this view. Richardson (1936), on the other hand, uses a raised fœtal heart rate as a diagnostic sign of premature separation of the placenta in the differential

diagnosis of ante-partum hæmorrhage, and holds that it precedes fœtal anoxia.

Irregularity in rhythm is difficult to assess, as minor irregularities are common, and unless they are associated with slowing would seem to be of little significance. However, Clemetson (1953) lists it as an indication of fœtal anoxia.

In the 217 cases of meconium staining investigated, the changes observed in the fœtal heart rate were as follows: (i) less than 110 per minute or a drop of 20 per minute, 52 cases; (ii) more than 160 per minute or a rise of 20 per minute, 17 cases; (iii) irregularity, five cases. In group (i), 26 infants required resuscitation; in group (ii), three required resuscitation; in group (iii) all required resuscitation, but in three of them the irregularity was associated with slowing of the heart.

There were five intra-partum fœtal deaths; all the fœtuses had slowing of the heart without preliminary irregularity or rise in heart rate.

From this it seems to emerge that the only fœtal heart alteration of any practical significance is a rate below 110 per minute, although it would seem logical to add a fall of 20 beats per minute as a rider to this. These rates should be taken between contractions, although Seward (1950) holds that a fall in fœtal heart rate below 10 beats per minute during a contraction is abnormal and indicates a decreased placental reserve or early anoxia.

## Conclusions on Management.

*Assessment of Case.*

The position should be assessed by the following measures: (i) careful auscultation of the fœtal heart, (ii) examination of the patient for possible causes of fœtal anoxia, (iii) vaginal examination to exclude prolapsed cord and to determine accurately the degree of dilatation of the cervix.

*Grouping of Cases.*

The cases, having been assessed, should fall into one of the following groups: Group I: meconium staining, with no other evidence or demonstrable cause of anoxia. Group II: meconium staining, with no other evidence of, but with a possible cause of anoxia. Group III: meconium staining, with other evidence of anoxia (slowing of the fœtal heart), with or without a possible cause of anoxia.

*Treatment.*

In group I a careful watch should be kept for any slowing of the fœtal heart. Everything should be in readiness for immediate forceps delivery or Cæsarean section in case either of these procedures becomes necessary. Should there be any other signs of fœtal distress, th n the case enters group III and the treatment is given accordingly.

In group II the treatment forms the most difficult problem and a number of factors must be considered. This group should be further subdivided, as follows: (*a*) those cases in which immediate delivery *per vaginam* is possible with relative ease and safety; (*b*) those which would be difficult and possibly dangerous vaginal deliveries, or in which Cæsarean section will be required. In group (*a*) the patients should be delivered at once. Those in group (*b*) should be treated with watchful expectancy, unless one or more of the following factors are operative, when immediate delivery is indicated: (i) The mother's condition indicates immediate delivery. (ii) The cord has prolapsed. (iii) The fœtus is a so-called "precious babe". (iv) Severe preeclampsia is present, especially if albuminuria has been present for several days. (v) A trial of labour has been given. (vi) There is a reasonable certainty of post-maturity.

Clayton (1953) states that "any suspicion of fœtal distress [in post-maturity] would justify immediate delivery, even section if the second stage has not been reached".

In group III, on the whole the patients should be delivered immediately, either by the application of forceps or by Cæsarean section.

One must constantly remember that the congested cerebral veins of the anoxic fœtus tear much more readily than the veins of the fully oxygenated fœtus. Particular care and gentleness must therefore be used during delivery, and I would be inclined to favour Cæsarean section when a difficult application of forceps seems likely.

*Oxygen Therapy.*—Oxygen should be immediately given to the mother, as there seems little doubt that this is of benefit to the fœtus. This view is strongly held by Lund (1941), by Seward (1950), by Clemetson (1953) and by Greenhill (1947*b*). It is Lund's opinion (1941, 1943*b*) that should the fœtal heart return to normal during the administration of oxygen, nothing further should be done. No operative intervention should take place without adequate oxygenation of the mother.

*Chloroform.*—When there is associated tetanic uterine contractions, careful use of chloroform may be of value.

*Analgesia.*—Nitrous oxide and oxygen should be used more often than it is, as both analgesia and maternal oxygen tension are improved by its use. The use of nitrous oxide and air should be discontinued at the slightest suggestion of fœtal distress. There have been encouraging reports on the use of n-allyl-normorphine in combating the respiratory depressant effects of the morphine group of drugs (Eckenhoff *et alii*, 1952). This may well relieve the fear of their use during labour.

*Anæsthesia.*—Anæsthesia should be chosen with care and given with high oxygen concentration, and the airways should be kept well cleared.

*Resuscitation.*—Davies and Potter (1946) make the following statement about resuscitation:

> In intrauterine fœtal distress with its associated anoxia the excitation of the respiratory mechanism results in exaggerated respiratory efforts and the aspiration of large amounts of amniotic fluids.

When this contains thick, tenacious meconium it can be very difficult to remove, and therefore the doctor should always be at the birth and be ready to resort to tracheal intubation if necessary. All other requirements for resuscitation should obviously be at hand.


## Summary.

1. The significance and management of meconium staining of the liquor during labour are discussed.

2. Some 4350 consecutive case histories have been analysed.

3. The ætiology and diagnosis of fœtal anoxia are important factors in the management and have therefore been briefly discussed.

4. It is considered that the appearance of fresh meconium during labour and a falling fœtal heart rate are the most useful clinical signs of fœtal anoxia.

5. The management of meconium staining during labour which I adopt is as follows: (*a*) Watchful expectancy when there is neither apparent cause for anoxia nor associated signs of it. (*b*) Immediate delivery when there are associated signs of anoxia. (*c*) When there is a cause for anoxia, but no associated signs of it, immediate delivery when this can be readily effected; otherwise watchful expectancy, except when special factors are operative.



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## A DYNAMIC TECHNIQUE FOR THE INDUCTION OF HYPNOSIS.

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During the last decade there has been a great increase in the use of hypnosis in medicine, and with it has come a very remarkable change in the way in which hypnosis is actually used in therapy. The change has been from symptom removal by suggestion to the analysis and working through of the unconscious conflicts which cause the patient's illness. Suggestive therapeutics has given way to hypnoanalysis. Instead of simple prestige suggestions, we are confronted with all the complexities of the psychodynamics of waking psychotherapy, presented in a much more explosive fashion on account of the hypnotized state of the patient. In these circumstances it is natural that our attention should be focused on the dynamics of the therapeutic situation, rather than on the hypnosis itself. New insights have been achieved. Authoritative attitudes to the patient have given way to a constantly passive relationship. Much work has been done on the problem of giving the patient understanding of the unconscious material recovered in hypnosis. But, on the other hand, in spite of these advances in our techniques in dealing with the hypnotized patient in therapy, it would seem that little progress has been made in the basic problem of the induction of hypnosis.

It is well known that hypnosis may be induced by a great number of different methods. However, a survey of recent literature suggests that most therapists, while acknowledging the fact that different methods can be used, seem to persist in the use of some particular technique to which they have become accustomed (Gindes, 1951; Brenman and Gill, 1947; Le Cron, 1952; Wolberg, 1948). This tendency is so pronounced that any modification of technique tends to become known by the name of the therapist who habitually practises it. This is a rather static approach to the process of induction of hypnosis, which contrasts with the essentially dynamic attitude which is being developed towards therapy with the hypnotized patient (Wolberg, 1945; Lindner, 1945; Schneck, 1953). The present paper aims to describe a method for the induction of hypnosis which employs the dynamic principles that have become accepted in other fields of psychiatry.

### Classical Methods.

The basic mechanism of the methods commonly used in medical practice involves the process by which the patient is subjected to a series of suggestions which are carefully graded as to ease of acceptance. Most of the techniques are variations of induction by suggestions of relaxation, as outlined by Bernheim in his classical description (Bernheim, 1947), or variations of induction by arm levitation, as described by Wolberg (1948). Both methods are modified by variation in the therapist's attitude in relation to authority and passivity. Induction by suggestions of relaxation can be further varied by fixation of gaze, as in Braid's method (Braid, 1899) or its modifications; Rosen's sensorimotor method (Rosen, 1953) is slightly different, as it exploits the spontaneous movements of the patient in a dynamic way. By using any of these methods, we know that a certain percentage of patients can be hypnotized to varying depths of hypnosis. The proportion of susceptible patients has been discussed by Bramwell (1930), and more recently reviewed by Hull (1933).

When difficulty is experienced in the induction of hypnosis, it would seem to be the accepted practice that the suggestions should be repeated many times, with suitable variation and, if necessary, over a number of sessions. We know that many patients who are at first resistive can be subsequently hypnotized by this technique.

#### *Criticism of the Classical Methods.*

Let us examine some of the dynamics of the induction of hypnosis by such procedures.

Hypnosis involves the loss of ego control. The ego defences may be overwhelmed by authority and prestige, as in the older school of medical hypnosis (Bernheim, 1947). Alternatively, the patient may be encouraged to surrender his ego control voluntarily. This may be achieved by the painstaking repetition of graded suggestions, during which the therapist maintains a constantly passive attitude. In this case the defences are simply whittled down. Both these methods approach the defences directly; the former by powerful onslaught, and the latter by slow attrition. It is clear that neither method exploits the psychological possibilities of the situation. The reasons why the patient is not accepting the suggestions are not considered. No notice is taken of the patient's need to defend himself against hypnosis, nor is any consideration given to the specific mechanisms which operate to fulfil the patient's need to defend himself. The patient is either hypnotized or not, according to the effectiveness of certain specific defences of the patient against certain specific suggestions of the therapist. In other words, it is an essentially static situation.

### Dynamic Principles.

The fact that the patient consciously desires to be hypnotized, and is prepared to cooperate fully in the induction process, is often not enough to ensure hypnosis. If the loss of ego control is interpreted as a threat, unconscious defence mechanisms are called into play to counter the threat. These defences against hypnosis can be roughly grouped under restlessness, negativism, simulation, depreciation and sleep. They have been described in some detail in another paper (Meares, 1954*b*). The aim of the present article is to describe a method by which these

defences can be integrated into a technique for the induction of hypnosis. At the same time, the passivity of the therapist, which is so important in hypnoanalysis (Wolberg, 1945; Lindner, 1945) and hypnography (Meares, 1954*a*), is maintained.

### The Dynamic Method.

There are two essential prerequisites for this technique: the therapist must have *rapport* with the patient, and the patient must really desire hypnosis.

In this method, as distinct from standard practice, the exact form of the initial suggestions is unimportant. As a matter of convenience, patients who relax easily are usually started with suggestions of relaxation, and those who exhibit increased muscle tone are given initial suggestions of arm levitation (Meares, 1954*e*). In the dynamic approach to the problems of induction, any delay in the process of hypnosis is to be considered in the light of unconscious psychological defence mechanisms. The technique aims to turn the patient's defences against him and use them in the hypnotic induction. In actual practice, it is remarkable how often this can be done. A patient being given suggestions of relaxation may make little fidgeting movements. This restlessness is purposive. The idea of complete relaxation carries with it the notion of immobility. By unconscious movement the patient is defending himself against the suggestion of immobility. Instead of the therapist's meeting the situation by emphasizing the suggestions of relaxation, the patient's attention is directed to his restlessness with the object of using it in the hypnotic process: "It is easy, it is coming all through you, your fingers are twitching, they are twitching, they are twitching more and more." As the restlessness is unconsciously motivated, the patient is unable to stop it by exercise of will. This phenomenon is now exploited. The suggestions are switched from relaxation to movement: "Your fingers are twitching, they are moving, they are tingling, they feel light, they are light, so light, the lightness is all through your hands, so light they are lifting into the air." The patient's defence has been turned against him by a swift change from suggestions of relaxation to levitation.

The same principles apply if the initial method is arm levitation. When suggestions of lightness of the arms are given, patients not uncommonly defend themselves by slumping forward and falling asleep. Such sleep is purposive. The patient is defending himself from suggestions of automatic movement by lapsing into the immobility of sleep. An immediate change is made to suggestions of relaxation and drowsiness, and soon the patient is in the sleep of deep hypnosis. If desirable, a return can now be made to the suggestions of arm levitation, which will now be accepted.

Other defences are treated in a similar way. The purposive nature of defence by negativism (Meares, 1954*b*) is quite obvious. So as to be quite sure that he does not accept the suggestions, the patient gives the opposite of the suggested response. By emphasizing in this way that he does not accept the suggestion, the patient does at the same time respond to the suggestion, although it is in a negative fashion. Because it does involve a response, the patient is encouraged in his defence, and suggestions are changed to an area which easily allows of negativistic behaviour. For instance, if arm levitation is being attempted, defence by negativism is recognized by the patient pushing down with his hands when suggestions of lightness are given. A change is made to repetitive movement of the arm. While his arm is held lightly by the sleeve, with the elbow resting on the table, he is given the suggestions: "Your arm moves back and forth, back and forth." At the same time the arm is gently moved back and forth by pulling on the sleeve. Soon it is noticed that the arm moves back on the suggestion of forward movement, and forward on the suggestion of backward movement. When the negativistic response is well established, the patient is challenged to stop the movement. The to-and-fro motion persists. He is unable to control the movement of his arm. He has been hypnotized by using his own defence to establish the automatic movements. Hypnosis can now be deepened by suggesting: "Your eyes are opening, but you won't wake up from it; your eyes are opening, but you won't wake up from it." The eyes open and invariably look away from the moving arm. The gaze is now directed to the uncontrolled movement of the hand. "Your eyes watch your hand, your eyes watch your hand." The witnessing of hypnotic phenomena in the self is a potent method of increasing the depth of hypnosis.

Similar principles are applied to meet defence by simulation (Meares, 1954*b*). Although the patient is not fully aware of what he is doing, this is a defence at a near conscious level. The patient tries to stop himself being hypnotized by voluntarily doing everything the therapist suggests. By following the suggestions voluntarily the patient feels that he acts of his own free will and therefore avoids being hypnotized. The fact remains that, although he does it consciously and intentionally, he is still responding to suggestion, and if he is allowed to continue in his defence he is soon hypnotized. Defence by simulation is recognized by the too rapid response to suggestions. If drowsiness is suggested, the eyes close immediately; if arm levitation is suggested, the arms straightway lift into the air. When this happens, the suggestions are modified to make the defence easy: "Your hands are light, they lift up into the air slowly and easily." "Now you feel a heaviness coming into them, they slowly go down again, slowly and easily." Other simple suggestions are given. They are followed easily and promptly. The therapist gives no sign that he realizes that the patient is not hypnotized. There must be no challenge, either direct or indirect. The therapist's only aim is to make it easy for the patient to continue his simulation. At the end of the session the patient is dismissed without being given an opportunity to involve the therapist in discussion. The procedure is repeated in a second session. Soon it is noticed that the patient's responses are slower; his gaze becomes fixed; there is an absence of the normal blinking of the eyelids. These are the signs that the patient is becoming hypnotized. Oblique challenges can be introduced. They are not accepted. Then the patient can be directly challenged to put his hands down. Both agonist and antagonist muscles contract, and he finds he cannot move his arms. Up till now the patient has believed that he has been acting of his own free will, and the sudden realization that he is in fact hypnotized may produce an anxiety reaction which is usually controlled quite easily by further increasing the depth of hypnosis (Meares, 1954*g*). The patient has been hypnotized by using his own defence to induce hypnosis. This is the dynamic approach in contrast to the older methods, in which a fresh start is made after pointing out to the patient that he is simulating.

With this dynamic method of induction there is no overwhelming of the patient with authority or prestige; there is no wearing down by the monotonous repetition of the same suggestion. Proper *rapport* is established prior to hypnosis (Meares, 1954*c*), so that the patient has confidence and really desires to be hypnotized. The initial interview can be so constructed as to facilitate the subsequent induction of hypnosis (Meares, 1954*e*), and a good clinical estimation of suggestibility can be made (Meares, 1954*e*). Many of the suggestions are given by non-verbal (Meares, 1954*f*) and extra-verbal (Meares, 1954*g*) means. The aim is that the patient should be merely helped and guided by the therapist, so that ego control is abandoned voluntarily. All the time the emphasis is: "You do it yourself, I only help you." The explanation of any hesitancy in the acceptance of suggestions, any delay in the process of hypnosis, is sought in the light of unconscious defence mechanisms. Immediately defences come into play, a change of technique is made. The primary object is to use the patient's defences in the hypnotic process. If this is not possible, at least a change of technique is made so that the established defences of the patient are not applicable to the new technique. If further defences manifest themselves, a further change is made.

In the older techniques it was considered a sign of failure to have to change from one method to another; in this technique one expects to keep changing all the

time until the patient is fully hypnotized. The passivity of the therapist is maintained throughout. It is interesting that many procedures which in the past have been used as a means of exerting blatant authority can in fact be used quite passively. Even the direct stare technique, which has been regarded as the most potent means of overpowering the patient, can be used passively. If the patient is told, "You look at me and it makes it easier to let yourself go; look at me and you can let yourself drift into it", he no longer has the feeling of being overwhelmed by the strength of will of the therapist, but only the feeling of being helped and guided by him.

Challenging can be quite a problem in relation to the passivity of the therapist. It is undoubtedly a very potent means of increasing the depth of hypnosis; but in the old school it is associated with ideas of mastering the patient. The concept of a passive challenge is almost a contradiction in terms, but a challenge can be expressed without overpowering authority: "You let yourself go; all your muscles relax; you do it yourself, I only help you; everything lets go; your legs are relaxed and heavy; you feel the heaviness in them; you do it yourself; you let yourself go; it's easy; your legs are heavy; they are so heavy now, so heavy that you cannot move them." When the suggestions are expressed in these terms the patient allows himself to drift into such a state that he cannot move his legs. This is really voluntary abandonment of ego control which is the essence of passivity in hypnosis.

The whole procedure is dynamic. It necessitates very keen observation of the patient so that the therapist is immediately aware if the suggestions are not being fully accepted. This is not always easy. For instance, when given suggestions of relaxation, the patient may spontaneously close his eyes and appear very relaxed. If there is any doubt in the therapist's mind as to the effect that the suggestions are having on the patient, it is a good plan to touch the patient lightly on the hair. If the patient has just closed his eyes spontaneously and is not much influenced by the suggestions, there is always a flicker of the eyelids; if, on the other hand, he has been influenced, the eyelids remain immobile. Alternatively, the patient can be told: "I take your hand but you won't wake up from it." Whilst saying this, the therapist lifts the patient's hand into the air and lets it go. If the arm falls back completely relaxed, or if it shows signs of catalepsy, the patient has been influenced; but if the patient just lowers his arm slowly when it has been released it is a sign that the suggestions have not been accepted, and a change should be made to another technique. There may be some reluctance on the part of the therapist to make such tests for fear of disturbing the patient in the belief that he might be awakened from light hypnosis. However, experience suggests the contrary—that touching or passively moving the patient usually has the effect of enhancing the effect of the verbal suggestions rather than waking the patient.

Considerable effect can be gained by interspersing the specific suggestions, such as suggestions of relaxation, of heaviness or of lightness, with non-specific suggestions. The exact meaning of the non-specific suggestions is filled in by the patient according to his psychological needs of the moment; "drifting into it"—"It comes all through you"—these are commonly used suggestions of this type.

### Comment.

The foregoing account is on the level of clinical observation as opposed to controlled experimentation. Accordingly, no statistically significant figures are available; but, provided the prerequisites of *rapport* and a desire to be hypnotized are really fulfilled, it would seem that almost anyone can be hypnotized by the dynamic method. The therapist has the patient's confidence, and the patient desires to be hypnotized. It is essentially a procdure which helps the patient past his unconscious defences, and so helps him to abandon his ego control to hypnosis.


### Summary.

Hypnosis involves the abandonment of ego control. If the loss of ego control is interpreted as a threat, unconscious defence mechanisms come into play to prevent hypnosis. In the dynamic method these defences are incorporated into the suggestions so that they are used in the induction process, and thus become the means by which the patient is hypnotized.


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## A SPINAL TURNING FRAME AND ITS USE IN THE MANAGEMENT OF CERVICAL DISLOCATION.


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*Brisbane.*


THE dangers of recumbency, especially in paraplegia, are well known; so are the methods of their prevention, turning being the most important. In the past, turning patients with injured backs has required skilled manpower to be continually available. This is no longer so. The nursing of patients with all varieties of severe back injury has now been converted from a burdensome nightmare for all concerned to an easy routine task for nurses and a safe, comfortable experience for the patient. This achievement has been made possible by the invention of the turning frame. Its value cannot be too highly lauded; it is one of the major medical advances made in the last ten years. This note describes the variety used in the Brisbane Hospital orthopædic department over the last three years.

### The Frame.

Figure I diagrammatically illustrates the frame used.

The revolving stretchers are six feet eight inches long by one foot six inches wide, and covered by canvas on which is placed a rubber mattress. For turning, the patient is clamped between the two stretchers like meat in a sandwich. After the patient has been turned the top stretcher is removed and slid sideways onto a rack on the chassis.

Our first models were used for patients with thoracic and lumbar injuries. So delighted were we with the control obtained that subsequent frames were modified to nurse patients with neck injuries with skull traction in place. This demanded cannulation of the axle (suggested by Dr. J. Binnie, now of Kyogle), and elongation of the frame by one foot to accommodate the skull calipers. The

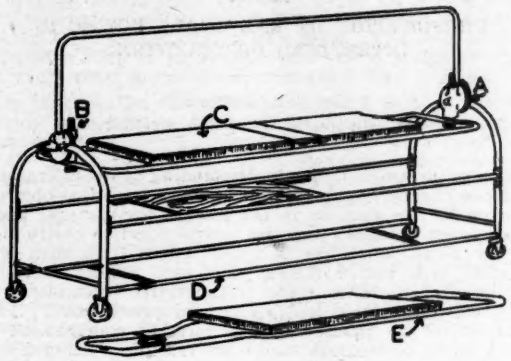


FIGURE I.

The turning frame. A, the axle mechanism; B, the bolt for the upper frame; C, the lower frame; D, the rack for the unused upper frame; E, the upper frame with face-piece.

width was also increased by six inches because some patients were afraid of falling.

The cannulated axle is shown in Figures II and III, and a patient *in situ* in Figure IV.

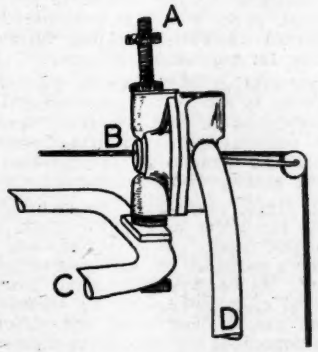


FIGURE II.

The cannulated axle. A, the bolt for the upper frame; B, the axle mechanism cannulated for the cervical traction cord; C, the lower frame; D, the chassis.

The patients are turned every two hours night and day, except for a four-hour period at night. Routine skin toilet and adequate fluid intake are maintained.

### Indications for Use.

The frame is used for the nursing of the following patients: (i) all paraplegics during the acute phase; (ii) all patients with severe back injuries; (iii) all patients suspected of having severe back injuries till X-ray evidence is available; (iv) patients who have had spinal grafts for varying periods after operation; (v) all patients requiring skull traction for neck injury, with or without quadriplegia.

### Advantages and Uses.

The frame can be managed by trainee nursing staff. One nurse can work the machine — two are desirable. Virtually no pain is felt by patients; they accustom themselves to the turn very quickly.

Bed sores never occur provided the patient's general health remains good. The only sores we have had in

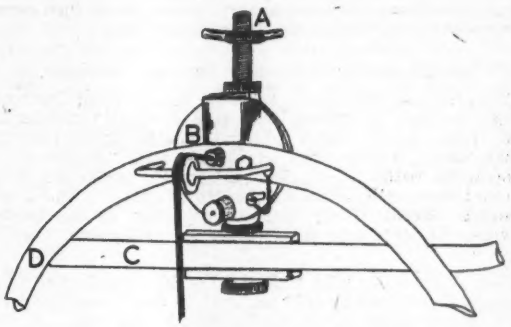


FIGURE III.

The cannulated axle. A, the bolt for the upper frame; B, the axle mechanism cannulated for the cervical traction cord; C, the lower frame; D, the chassis.

patients with cord transections have been terminal, with one exception. This occurred in a paraplegic male with a severe facial injury, which prevented two-hourly turning.

The mobility of the frame allows the patient to be wheeled to the X-ray department for adequate spinal X-ray examinations without his back being moved. This

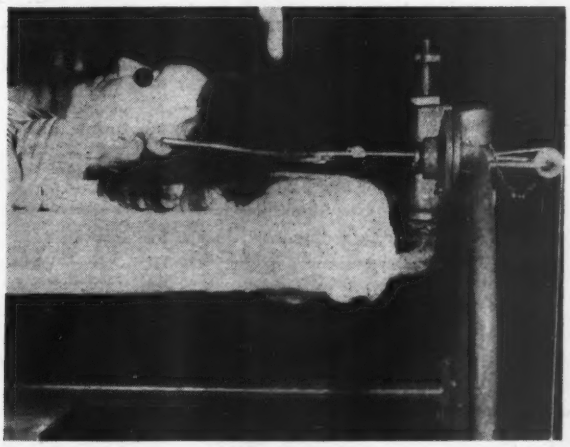

FIGURE IV.

The frame in use with cervical traction *in situ*.

is of extreme importance. We have had a patient referred with a partial paraplegia which occurred four days after the injury. The paraplegia was precipitated by posturing of the patient in an X-ray department in an effort to obtain good X-ray films. It is routine practice in this hospital for patients with severe (or suspected severe) spinal injury to be moved directly from the ambulance stretcher to the turning frame before any X-ray films are taken.

The frame can also be moved to the operating theatre and spinal surgery undertaken on it. We perform grafting operations in this fashion on patients with severe spinal injuries, especially if movement is likely to endanger the

spinal cord. The chassis is placed on blocks at a height convenient to the surgeon concerned.

Complete control of cervical injuries can be maintained by traction on the frame, and coincidently the advantages of turning are not lost. Blocks are used to raise the head of the bed if counterbalancing is needed or if the head-low position is found to be distressing. In this manner we have been able to follow the full recovery of a patient with almost total quadriplegia following a cervical dislocation without the development of bed sores, pneumonia or urinary tract infection or stone.

*Treatment of Dislocated Cervical Vertebræ.*

The frame, with skull traction by modified Pearson's tongs, is used to reduce dislocated cervical vertebræ and hold them until plaster fixation can be applied several weeks later. Intravenous anæsthesia with "Pentothal", in association with a relaxant, allows the reduction to be accomplished with almost finger-tip control. It also allows excellent lateral X-ray films to be taken of the seventh cervical vertebra and most times the first dorsal vertebra as well.

Ten dislocations with unilateral or bilateral locked facets have been reduced by this method; in most cases reduction has been effected by 30 to 40 pounds' traction. A little rotatory movement is also sometimes necessary. In one case only did the method fail. This was a case of bilateral locked facets with neural arch comminution. One facet only was reduced. The reduction was completed operatively.

No cord damage has been caused to date by these manipulations. The maximum traction used has been 80 pounds for half an hour.

### Disadvantages.

The frame cannot be used if there are severe associated injuries of the face and trunk; nor can it be used if injuries of the lower limb require traction.

Some obese patients are difficult to nurse on the frame. Because of this, our newer models are two feet wide and could even be a little wider. Very tall patients also find the smaller frames uncomfortable. All our future models will be made at least seven feet eight inches long by two feet wide.

Restless patients cannot be nursed on the frame unless well sedated. Patients with associated severe head injuries are unsuitable, as are senile and alcoholic patients.

### Summary.

1. A spinal turning frame and its use are described.
2. It is indicated for nursing patients with severe back injuries, paraplegics, patients who have undergone spinal grafting procedures after operation, and patients with cervical injuries requiring skull traction.
3. No strength or skill is needed to use the frame. It is believed that the principle embodied in this frame is the answer to the problem of the safe comfortable turning by untrained personnel of patients with back injuries.
4. The frame prevents the formation of bed sores and facilitates their cure if they are already present.
5. X-ray films can be taken and operations performed on it without moving the patient.
6. Cervical dislocations can be reduced with it, skull traction maintained thereafter, and the patient still be turned.
7. The frame cannot be used if there are severe associated injuries of the face, trunk or lower limbs, or if the patient is very obese, old or restless.

### Acknowledgements.

I wish to thank Dr. A. D. D. Pye, General Superintendent of the Brisbane Hospital, whose interest in nursing problems has made these frames available, and to Mr. Arthur Birch, who has had a considerable first-hand experience of this spinal frame, for his diagrams. The frames were made by the Queensland Bedstead Company, Proprietary, Limited, of Milton, Brisbane, whose cooperation is gratefully acknowledged.

## Reports of Cases.

### PERFORATION OF THE SMALL BOWEL IN INTESTINAL OBSTRUCTION.

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RECENT ADVANCES in our understanding of the alterations in blood chemistry occurring in cases of intestinal obstruction enable the surgeon to compensate for many of these biochemical changes; thus the patient survives obstruction to the small bowel for a much longer time than was possible even ten or fifteen years ago. These additions to knowledge have made conservative treatment of intestinal obstruction feasible in appropriate cases. However, there are hazards in this form of management of small bowel obstruction: some are relatively common and are therefore well known; others are less well recognized and therefore deserve special attention.

The present report details two fatal cases of multiple perforation of the small bowel occurring as a complication of long-continued intestinal obstruction. Prolonged distension of the bowel appears to play the major role in the evolution of this complication, and avoidance of prolonged distension should be recognized as an important principle in the conservative management of intestinal obstruction.

It is not astonishing to find that reports of perforation complicating prolonged obstruction to the small bowel are rare in the literature. Before the fluid and electrolyte disturbances initiated by obstruction to the small bowel were understood, patients seldom survived this condition (unless subjected to early surgical intervention) for sufficiently long for perforation to occur.

However, perforation of the ileum was not unknown. Frederick Treves, in his classical monograph on intestinal obstruction published in 1884, refers to several cases of small bowel perforation complicating obstruction, and warns against the danger of precipitating perforation when handling grossly distended bowel.

Van Beuren (1926) refers to a case of intestinal obstruction involving the lower part of the ileum in a woman, aged thirty-eight years. This patient was treated conservatively for a period of six days before being subjected to laparotomy. At operation the small bowel was found to have several dark patches on its surface (suggesting necrosis), and one of these areas had perforated. From van Beuren's notes it is not possible to decide whether this perforation had been spontaneous or had been induced by operative manipulations.

In an attempt to elucidate the mechanism of perforation, van Beuren produced experimental intestinal obstruction in a series of dogs. In these experiments he was able to reproduce not only the hæmorrhagic areas, but also free perforation similar to that found in his clinical case. As a result of these experiments he concluded that distension played a major role in the causation of perforation in the small intestine.

Wangensteen (1942), in his book on intestinal obstruction, describes in detail the results of the extensive experimental work carried out on the subject. However, while he refers to the occurrence of necrosis and perforation of the bowel wall in the experimental animal, he gives no indication of the complication having been seen in the human subject.

Clearly perforation of the small bowel associated with obstruction is a different lesion from perforation of the

rare primary jejunal ulcer. The literature in this second subject has been reviewed in two papers by Smith (1935) and Ebeling (1933).

The histories of the two cases forming the basis of this paper are as follows.

### Case I.

A., a male patient, aged thirty-eight years, was admitted to hospital with a history of pain in the right iliac fossa of six hours' duration. This pain had begun gradually, and he had vomited once at the onset. The past history included a story of vague dyspepsia over a period of some six weeks prior to the onset of his right iliac fossa pain.

On examination, the patient was found to be a healthy looking man with a pulse rate of 82 per minute and a temperature of 99·4° F. Abdominal signs were restricted to the right iliac fossa, where definite tenderness and release tenderness were present. There was no rigidity, and the tenderness did not extend higher than the level of the iliac crest.

A provisional diagnosis of acute appendicitis was made, and the abdomen was opened by a McBurney's incision. When the peritoneum was opened, a quantity of glairy clear fluid was observed, the appendix was found to be normal, and it was considered that the diagnosis was probably that of a perforated peptic ulcer. An upper paramedian incision proved this to be so, the ulcer was oversewn, fluid was removed from the peritoneum, and the abdomen was closed, a drainage tube being left in the pelvis.

The pelvic drainage tube was removed on the second day. Convalescence was uneventful until the thirteenth day after operation, when vomiting occurred after the patient's evening meal. When vomiting occurred again on the fourteenth day, a Rehfuss tube was passed and intravenous therapy was begun. Examination of the abdomen at this time demonstrated slight lower abdominal distension, and questioning of the patient revealed that neither flatus nor fæces had been passed in the preceding twenty-four hours. A diagnosis of acute intestinal obstruction was made, and in the absence of a story of pain and the signs of abdominal tenderness and rigidity, conservative treatment was decided upon.

A plain X-ray film of the abdomen taken on the fifteenth day showed that three coils of distended small bowel were present in the pelvis. The abdominal distension by this time had increased and was obvious in the lower part of the abdomen. However, the patient's general condition remained satisfactory and, in spite of the persisting distension, conservative management was continued. He remained in this state until the twenty-second day after operation (that is, nine days after the onset of the obstruction). On that day he complained of sudden, severe, generalized abdominal pain, and peripheral circulatory failure rapidly developed. Energetic resuscitation enabled laparotomy to be performed six hours after the onset of pain.

At operation 12 pints of intestinal content and peritoneal exudate were removed from the abdominal cavity. The small bowel was found to be obstructed by adhesions in the pelvis, and about six feet of empty but extremely dilated small bowel were found immediately above this obstruction (the bowel above this six foot segment was only moderately dilated). Scattered along the length of this segment were at least 50 dark hæmorrhagic necrotic areas measuring about five by three millimetres on their surface area. While these occurred over the whole surface of the bowel, their maximum incidence was on the antimesenteric border. Twelve of these areas had perforated and leaked intestinal content when the bowel was manipulated.

The obstructing adhesions were divided, the perforated areas were oversewn and the abdomen was rapidly closed. However, the patient died two hours after operation, failing to regain consciousness after the anæsthetic. No post-mortem examination was available.

### Case II.

A male patient, aged seventeen years, was admitted to hospital with a typical history of acute appendicitis of twelve hours' duration. Examination indicated that the diagnosis of appendicitis was accurate, and that perforation with local peritonitis had developed.

Laparotomy by McBurney's incision confirmed these findings, appendicectomy was performed, and the abdomen was closed.

After operation his convalescence was unsatisfactory. Lower abdominal distension gradually developed, and suction and intravenous therapy were proceeded with. The amount aspirated was never great, although there was a complete absence of the passage of flatus and fæces. No X-ray picture was taken in this case, but on clinical grounds it appeared that the obstruction was in the lower part of the ileum. On the seventh day after operation the patient complained of some mild lower abdominal colic, and the abdominal distension increased.

On the tenth day after operation he complained of sudden severe generalized abdominal pain, and peripheral circulatory failure rapidly developed. Resuscitation was followed by laparotomy, at which the findings were similar to those described in Case I. Much free fluid and exudate was removed from the peritoneal cavity. The lower four feet of ileum were grossly dilated but practically empty. Along the surface of the bowel were many necrotic areas, a number of which had perforated. The obstruction was due to adhesions in the ileo-caecal area. The perforations were rapidly oversewn and the abdomen was closed; but the patient survived for only three hours after operation. Again no post-mortem examination was available.

### Discussion.

It is to be observed that in both these cases prolonged distension ultimately led to the development of patchy necrosis and perforation of the bowel wall.

Perforation of the bowel complicating intestinal obstruction is of infrequent occurrence, and in the vast majority of such cases is associated with acute occlusion of the large bowel. It is well recognized that when perforation complicates colonic obstruction the caecum is the site most frequently affected, and it is highly significant that the caecum is usually found to be the site of maximal distension in this condition. A further feature worthy of note is that caecal perforation occurs relatively late in the course of the disease, and so it would appear that both the degree of distension and the time during which that distension persists are of importance in determining the occurrence of caecal perforation. Moreover, the caecum may perforate in one or more sites simultaneously, and it is not unusual to find many areas of doubtful viability in the wall of a caecum which has perforated (Saeltzer and Rhodes, 1935). The resemblance of these findings to those in the two examples of small bowel perforation described above is obvious, and it is probable that the factors determining perforation are similar in both of these lesions.

When one attempts to analyse the case histories given in the present report, it becomes clear that the following features are common to both: (*a*) the small bowel was grossly distended; (*b*) the distension had persisted for several days; (*c*) many areas of impaired viability were present, scattered throughout the wall of several feet of small bowel; in each case only a few of these areas had actually perforated.

It would appear, then, that the prolonged distension had resulted in the almost simultaneous development of many necrotic areas in the bowel wall, and that reactive changes had led to perforation in some of these necrotic areas. It is clear that necrosis of the bowel wall associated with obstruction may be due either to interference with its blood supply, or to the damaging action of the intestinal bacteria, or to a combination of both of these factors. Experimental evidence would support the hypothesis that vascular factors were of prime importance in the development of these lesions. Van Beuren (1926), by producing

experimental intestinal obstruction in dogs, was able to demonstrate that these necrotic areas could be produced at will. While they occurred at all sites in the bowel wall, the necrotic areas were at maximum concentration on the antemesenteric border—that is, at the point farthest removed from the site of blood supply to the wall. Moreover, van Beuren showed that the vessels in these necrotic areas were occluded by recent thrombus, whereas those supplying neighbouring viable areas were not so obstructed. That these findings are not peculiar to the experimental animal is also clear from reference to van Beuren's paper; he gives excellent illustrations of similar areas of patchy necrosis associated with thrombosed vessels in the single case of perforation of the human intestine which he describes. When discussing the manner in which distension produces vascular obstruction, van Beuren pointed out that the circumference of the bowel wall was approximately three and one-seventh times its diameter, and that, therefore, a given increment in diameter of the bowel would produce an elongation of the vessels in its wall of at least three times that amount. Further, the vessels tend to become obstructed as they pass through the layers of the bowel wall to ramify in the deeper structures, and van Beuren concluded that these factors were sufficient to produce the vessel obstruction referred to above.

Sperling and Wangensteen (1935) carried the experimental investigation of this complication further. They measured the intra-enteric pressure in a series of patients suffering from small bowel obstruction, and then reproduced these pressures in a closed ileal loop in the dog. They were able to maintain the intra-enteric pressures at predetermined levels for many hours, and showed conclusively that while the bowel wall remained viable during the first fifteen to twenty hours after application of pressure, necrosis developed if that pressure was maintained for periods of twenty to thirty hours. Moreover, it was found that the bowel gradually distended with the passage of time, and that the occurrence of necrosis in the bowel wall was related to the degree of distension. In view of the ease with which necrotic areas and perforation of the bowel can be produced in the experimental animal, it is surprising that the literature presents so few examples of its occurrence in the human subject. The rarity of this condition is certainly more apparent than real: intestinal obstruction is a condition dealt with by many surgeons and general practitioners, and it is probable that most examples of this uncommon complication remain unrecorded.

The complication, albeit uncommon, must be recognized as a possibility whenever prolonged distension of a loop or loops of small bowel is allowed to occur. It would appear that, in order to reach the degree of distension necessary to precipitate perforation, only a limited length of small intestine must be dilated.

In paralytic ileus, in which prolonged distension of the bowel is common, it is known that perforation is rare. The reasons for this are probably twofold: (i) If the distension becomes gross and involves the whole of the small intestine, the attendant biochemical disturbances are such that early death occurs—that is, before perforation has time to develop. (ii) In uniform distension of the intestine, the abdominal parieties impose a limiting factor whereby gross distension of any isolated loop becomes impossible.

McIver (1933), when discussing the various types of experimentally produced intestinal obstruction, points out that the circumstances most likely to produce perforation of the bowel are found when an isolated loop of intestine is obstructed, its mesentery and blood supply remaining intact. Under these circumstances the single loop becomes progressively distended until patchy necrosis and perforation develop. In cases of simple obstruction it is uncommon to see the degree of distension which occurs in the isolated loop, and therefore perforation is also rare. The isolated loop with obstruction to its mesenteric vessels presents a further variation in the mechanical arrangement. In this case, as is well known from experience with strangulated intestine, massive (rather than patchy) gangrene of the bowel wall develops. McIvor states that there is no comparable state of affairs to the experimental isolated loop seen in human disease.

In considering the sequence of events leading up to perforation of the intestine in the present two cases, it would appear reasonable to assume that a double obstruction occurred, so that an isolated obstructed loop was produced. Gastric aspiration would control the distension in the bowel above the proximal obstructing agent, but could not deflate the loop between the two obstructions, which therefore become grossly distended.

Obviously the lesson in these cases is that, when local distension of the bowel fails to be relieved by intestinal aspiration in a case of intestinal obstruction treated conservatively, laparotomy should be undertaken to determine whether a closed loop of bowel is present and to relieve such condition should it exist.

### Summary.

1. Two cases of perforation of the bowel complicating long-continued intestinal obstruction are described.

2. A brief review of the literature is given, including that relating to experimental work on this complication.

3. The importance of prolonged distension of a localized segment of small bowel in the evolution of perforation is stressed.

4. It is clear that the avoidance of prolonged local distension, in that it may indicate the development of a "closed loop" type of obstruction, is an essential feature of the conservative management of intestinal obstruction. The loop of intestine obstructed at its proximal and distal end is the one most likely to develop patches of necrosis and so perforate. Therefore, prolonged local distension is an indication for laparotomy in conservatively treated intestinal obstruction.

### Acknowledgement.

I wish to thank the honorary medical staff of the Royal Melbourne Hospital for permission to publish these two cases of intestinal perforation.

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## NON-INDUSTRIAL LEAD POISONING: A REPORT OF 25 CASES.

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In modern times it might be considered that, owing to improvements in water supply, legislation in regard to food containers, abandonment of old methods of wine clarification and of other practices by which lead could be ingested, and decreasing use of drugs containing lead, lead poisoning of non-occupational origin was so rare as to be not worthy of serious consideration. However, in

TABLE I.

| Case No. | Particulars of Patient. | Occupation, if Any. | Source of Lead. | Results of Laboratory Tests. | | | | Main Symptoms and Outcome. |
|---|---|---|---|---|---|---|---|---|
| | | | | Blood Tests. (Stippled cells and polychromasia cell counts expressed per 1,000,000 red cells. | Coproporphyrin. (Milligrammes per Litre of Urine.) | Lead in Urine. (Milligrammes per Litre.) | Lead in Blood. (Milligrammes per 100 Grammes.) | |
| 1 | Baby (breast fed). | —— | Ointment used for cracked nipples. | Stipple cell count, 35,300; ratio, 2·95. | — | 0·47 | — | Severe anæmia, debility, recovery. |
| 2 | Mother of baby (Case 1). | Housewife. | Same ointment as in Case 1. | —— | — | 0·17 | — | Unknown, but reported that lead poisoning developed shortly after test performed. |
| 3 | Boy, aged seven years. | —— | Pills supplied by Chinese herbalist for treating asthma. Lead ingested probably 22 milligrammes per day for a year. | Hæmoglobin value, 60% to 70%; stipple cell count, 51,700; ratio, 0·50. | — | 0·29 | — | Bilateral foot-drop, present four years later. |
| 4 | Male. | Dentist. | Unknown.[2] | Hæmoglobin value, 50%; stipple cell count, 43,500; ratio, 1·04. | — | 0·19 | — | Severe anæmia, recovery. |
| 5 | Female. | Housewife. | Pills supplied by Chinese herbalist. Lead ingested 154 milligrammes per day for three weeks. | Red blood cell count, 3,300,000 per cubic millimetre; hæmoglobin value, 61%; stipple cell count, 14,750. | — | — | — | Anæmia, recovery. |
| 6 | Boy, aged eleven years. | —— | Dirt eaten. | Stipple cell count, 10,000; ratio, 3·21. | — | 0·12 (0·24 while on citrate therapy.) | — | Paralysis, recovery. |
| 7 | Baby, aged twenty months. | —— | Probably lead oxide used for cement for repair of optical instruments. | Stipple cell count, 4,350; ratio, 1·73. | — | 0·28 | 0·10 | Debility, recovery. |
| 8 | Boy. | —— | Dirt eaten. | Stipple cell count, 15,900; ratio, 1·81. | — | 0·14 | — | Convulsions, recovery. |
| 9 | Boy, aged eight years. | —— | Probably water supply from tank. | Stipple cell count, 3,450. | — | 0·16 | — | Debility, loss of appetite. |
| 10 | Girl, aged five years, sister of boy in Case 9. | —— | Probably water supply from tank. | Stipple cell count, 6,250. | — | 0·13 | — | Debility, loss of appetite. |
| 11 | Girl, aged two years. | —— | Probably hot water system: lead connexions. | Red blood cell count, 2,850,000 per cubic millimetre; hæmoglobin value, 62%; stipple cell count, 16,800; ratio, 0·45. | — | — | — | Debility, loss of appetite. |
| 12 | Girl, aged four years.[1] | —— | Colours used in kindergarten. | —— | — | — | — | Convulsions, death. |
| 13 | Girl, aged three and a half years.[1] | —— | White lead paint off outside of walls of house. Designs rubbed off with fingers moistened in mouth. | —— | 1·0 | — | — | Convulsions, death. |
| 14 | Boy.[1] | —— | Dirt eaten, and water. | —— | — | — | — | Convulsions, death. |
| 15 | Male, aged twenty-one years. | Grocer's assistant. | Lead foil and metallic lead chewed to form pellets for shanghai (catapult). | Hæmoglobin value, 61%; stipple cell count, 15,600; ratio, 2·3. | 1·6 | 0·15 | 0·13 | Bilateral wrist drop, anæmia, recovery. |
| 16 | Female. | Nursing sister. | Unknown (possibly water supply). | —— | 2·4 | 0·43 | — | —— |
| 17 | Male. | Grocer's assistant. | Chinese herbalist's remedies. | Red blood cell count, 4,960,000 per cubic millimetre; hæmoglobin value, 65%; stipple cell count, 34,200; ratio, 1·5. | 0·75 | 0·53 | 0·15 | Anæmia, weakness, abdominal pain, recovery. |

TABLE I.—*Continued.*

| Case No. | Particulars of Patient. | Occupation, if Any. | Source of Lead. | Results of Laboratory Tests. | | | | Main Symptoms and Outcome. |
|---|---|---|---|---|---|---|---|---|
| | | | | Blood Tests. | Coproporphyrin. (Milligrammes per Litre of Urine.) | Lead in Urine. (Milligrammes per Litre.) | Lead in Blood. (Milligrammes per 100 Grammes.) | |
| 18 | Female. | Housewife. | Abortifacient (?). | Stipple cell count, 42,500, and polychromasic cells, 17,500; ratio, 8·2. | — | 0·18 | — | Abdominal colic, recovery. |
| 19 | Female, aged three years. | —— | Paint. | Stipple cell count, 3,000, and polychromasic cells, 3,000. | — | 0·05[4] | 0·05[4] | Encephalopathy, recovery. |
| 20 | Boy, aged eleven years. | —— | Paint (paint blisters eaten). | Stipple cell count, 13,900; ratio, 2·2. | — | 0·09 | 0·11 | Foot drop, anæmia, recovery. |
| 21 to 25 | Four children, one adult.[3] | Adult, housewife. | Lead dust and/or metallic lead scraps from adjacent factory polishing lead ornaments. | —— | | | —— | |

[1] See Table II for analyses of organs at coroner.

[2] In regard to Case 4, very extensive investigations were carried out in an attempt to trace the source of the lead. The water supply at the patient's professional chambers and at his residence (both that which had stood overnight in the pipes and the later runnings), the materials used for fillings, and lead excretion of other members of the family were all tested, but no source of lead was discovered. He had been in the habit for some considerable time of taking sodium bicarbonate regularly. This was found to contain no lead, but there was the possibility that such a régime liberated lead from storage in the bones, such lead having been deposited through ingestion from some unknown source years before.

[3] These cases reported by Bridges (1953).

[4] These results were for samples collected some weeks after exposure.

recent years, the Industrial Hygiene Division of the Victorian Health Department has investigated a sufficient number of cases of lead poisoning in adults in which the causes have not been industrial, and in children, to indicate the advisability of keeping lead in mind as an aetiological factor in ill-health.

Although there is nothing particularly novel in regard to clinical signs or symptoms in these cases, this Division has thought them of sufficient interest to bring them to the notice of the medical profession for two reasons. The first is to indicate the help which adequate laboratory investigations can give in these cases, and the second is to indicate that lead poisoning can be the result of quite unexpected causes.

Table I gives a short summary of these cases.

TABLE II.

*Analyses of Bones and Organs in Cases XII, XIII and XIV (Milligrammes per 100 Grammes of Fresh Tissue).*[1]

| Case Number. | Bone. | | Brain. | Liver. | Kidney. |
|---|---|---|---|---|---|
| 12 | —— | | 0·52 | — | — |
| 13 | Humerus near epiphysis | 20 | 0·42<br>0·46 | 3·3<br>3·5 | —<br>— |
| | Shafts | 4·8<br>4·7 | — | — | — |
| 14 | Femur near epiphysis | 23<br>28 | 0·29<br>0·33 | 5·4<br>5·6 | 2·2<br>2·3 |
| | Shaft | 1·5 | — | — | — |

[1] These values were all greatly in excess of normal and definitely indicated excessive absorption of lead.


### Acknowledgements.

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### Reference.


BRIDGES, A. (1953), "Lead Intoxication in Three Families", M. J. AUSTRALIA, 2: 62.


## Books Received.

*[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]*

"A Further Study in the Nature of Disease", by J. E. R. McDonagh, F.R.C.S.; 1954. London: William Heinemann (Medical Books), Limited. 8¼" x 6", pp. 388. Price: 21s.

This study deals with the influenza of 1950-1953, with rheumatism and with the ductless glands.

"Reflections on Renal Function", by James R. Robinson, M.D., Ph.D. (Cantab.); 1954. Oxford: Blackwell Scientific Publications. 9" x 5½", pp. 164, with three text figures. Price: 17s. 6d.

Intended to bridge the gap between the chapters in general text-book and larger treatises.

"Modern Treatment Year Book, 1955: A Year Book of Diagnosis and Treatment for the General Practitioner", edited by Cecil Wakeley, K.B.E., C.B., LL.D., M.Ch., D.Sc., F.R.C.S., F.R.S.E., F.R.S.A., F.A.C.S., F.R.A.C.S.; Twenty-First Edition; 1955. London: Published for the Medical Press by Baillière, Tindall and Cox, Limited. 9" x 6", pp. 370, with 45 illustrations. Price: 25s.

Contains some thirty-six articles written by specialists in their own subjects.

"Modern Surgery for Nurses", edited by F. Wilson Harlow, M.B., B.S. (Durham), F.R.C.S. (England); Third Edition; 1954. 8¼" x 6", pp. 396, with 419 illustrations. Price: 27s. 6d.

There are eleven contributors. The second edition was published in 1951.

The Medical Journal of Australia

SATURDAY, APRIL 30, 1955.

*All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.*

*References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those adopted by the Quarterly Cumulative Index Medicus. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.*

*Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.*

## THE BRITISH MEDICAL ASSOCIATION FLOOD RELIEF FUND.

THE response to the appeal by the Council of the New South Wales Branch for subscriptions to the fund set up to give relief to medical practitioners who suffered loss in the recent floods has been most disappointing. We cannot think that members have with clear deliberation turned a deaf ear to the call for help. To entertain such an idea would be to attribute to the great body of the profession selfishness and a lack of brotherly feeling of the worst kind. Rather must we suppose either that the appeal was not noticed or else that procrastination has once again robbed willingness of its effective action. To reemphasize the appeal the following statement published in the New South Wales Branch "Monthly Notice" is reproduced here.

> The results of the appeal, for assistance to doctors who suffered heavy financial loss through the recent floods, are remarkable for their meagreness.
>
> Members will be interested in the following details, which the Council of the Branch offers in support of a further request for donations.
>
> Some 35 members of the profession suffered flood losses, amounting to thousands of pounds in several instances, and in none to less than five hundred pounds. The special appeal made on 24th March has brought in £1854, received from only 340 contributors, though the membership of the Branch is 3805. In faraway Britain, members of the profession have for the same purpose collected £625, which is acknowledged with a deep sense of gratitude, as are also donations amounting to £69 7s. 6d. from seven members in other States, and a donation of £100 from an Australian practising in London.
>
> It is assumed, however, that response to the Association's appeal has been small because members may have already contributed to the public flood relief funds. Also, the plight of colleagues in the devastated areas may not be fully appreciated by other members. It is therefore pointed out that for many doctors flood damage involved homes, consulting rooms, equipment and cars. In addition, practitioners in the flooded regions worked without remuneration for about three weeks, considering themselves freely at the disposal of all who needed medical treatment.
>
> Wholesale pharmaceutical houses came to the aid of chemists who lost their stocks during the floods, restocking their pharmacies free of charge. In the same spirit, members of the Branch who have not already done so will wish to aid their colleagues in the devastated areas. Cheques for the purpose may be made payable to the "British Medical Association Flood Relief Fund".
>
> *Donations to the fund will be published in The Medical Journal of Australia.*

The example of the members of the Association in Great Britain cannot fail to arouse a warm feeling of gratitude. In the face of such generosity members in Australia and especially in New South Wales cannot "pass by on the other side". There is not a single member of the 3800 on the New South Wales list who could not afford to give at least one guinea, and who would not do so if he were asked personally to contribute. A personal, face-to-face appeal should not be needed.

## "WHY?" AND "HOW?"

WHEN a medical practitioner is called to the bedside of a patient, it is at once apparent to him that he has to do something. What he does will be the result of his medical up-bringing, his sense of proportion and his honesty of purpose. He will probably ask himself what is the matter with the patient—he will seek in his own mind some kind of a diagnosis. If he is true to the teaching he has received and the training he has undergone, if he wishes to do the best he can for his patient, he will try to discover the *fons et origo mali*. On the other hand, he may accept the surface picture as telling the whole story, looking on the symptoms as the only features which have to be got rid of. In the first instance he will be one of those who continually ask "Why?"; in the second he will be content with the query "How?". There is a world of difference between these two attitudes of mind, and most of us will do well to determine whether in our clinical work we shall accept the role of a constantly recurring interrogative or whether we shall be opportunists in our handling of patients, being content to remove unpleasant symptoms like a would-be gardener who plucks off a weed without looking for its roots.

Looking at the "How" and the "Why" attitudes of mind, we must remember that the "How", what we have called the opportunist, point of view may be thrust upon us—something must be done without delay in order to save the patient's life. For example, if the patient has had a severe hæmorrhage from the gastro-intestinal tract, nothing may be gained by delay in an attempt to determine the source of the bleeding, and a blood transfusion has to be given at once. Apart from emergencies of this kind, however, the "How" attitude is to be deplored. When the cause of a disease is unknown, symptomatic or empirical treatment cannot be avoided. When such treatment is given it should be with realization of its empiricism, and even then with full inquiry into the personal and environmental history of the affected person. It is not unlikely that such full inquiry may happen to reveal information that will throw light on the obscurity of the condition. In other words, the clinician in such circumstances must try to preserve an open and inquiring mind. If he does not do so, his treatment in other well

understood conditions is likely to degenerate. He may be like the practitioner recently mentioned in these columns who, faced with a patient who had a temperature of 105° F., gave an antibiotic drug, and when this failed in its purpose immediately switched to another. Only when the rise in temperature recurred and the patient was removed from the care of the clinician and admitted to hospital was a full history taken and an examination of the blood made which revealed an abundance of malarial parasites. The recurring "interrogative" would not allow this to happen—he would at least have discovered that the patient had been for some time in an area where malaria flourished. He would then have had an examination of the blood made; and it is unfortunately true that the other, the opportunist, type of practitioner might have given antimalarial medicaments before the parasites had actually been discovered. The practitioner who always asks "why", tries to discover the exact nature of the patient's infection or disability. He wants to know its cause, bacterial or metabolic or of other origin. He wants to know whether there is anything in the patient's environment or past history that rendered him liable to be affected by the ailment. He will want to discover whether other persons are affected and why. And he will ask himself whether in his treatment of his patient he cannot do something to prevent recurrence of the complaint or its spread to other persons. In other words, he is, in actual fact, a practitioner of preventive medicine.

The end of the whole matter is that the practitioner must not be afraid to acknowledge his ignorance, his ignorance which he shares with other followers of medicine. He must continually ask: "Why?" He may in this way acquire that "attitude of doubting, of questioning and of seeking after truth" which the late Frederic Wood Jones stated was rarely acquired as a result of our educational system. It is incontestably true that it is much more important to know the nature of a disease than to know how to cure it. If we know its nature we may be able to prevent it, and then there will be no need to cure it.

# Current Comment.

## THE TREATMENT OF ALCOHOLISM.

IN "Alcoholism", which is a general survey of the subject, Ian Gregory[1] gives an outline of the treatment of victims of this condition. The first stage he calls "disintoxication"; this is preliminary to attempts at arresting alcoholic drinking, and consists of the immediate treatment of acute alcoholic intoxication and the subsequent alleviation of the concomitant disorders of chronic alcoholism. It consists mainly of drug treatment; alcohol, insulin and glucose, liver and the vitamin *B* complex, ACTH and cortisone, amphetamine and strychnine, barbiturates, "Myanesin" and methylamine choline all may have a place in this stage. The next stage is the deterrent one, and it seems as if there is little of real value here. Hospitalization with supervision will be of use only for as long as it lasts, and may increase the craving and contribute to greater indulgence after it is over. Punitive measures, such as heavy fines or imprisonment, can have no lasting effect. Conditioned reflex treatment may be of value in selected cases, but its application is limited. Disulfiram ("Antabuse") requires the active cooperation of the patient, and the true addict cannot continually cooperate. It has the disadvantage that the alcohol-disulfiram reaction may cause collapse, and the reaction is much more severe in patients suffering from the very conditions which are commonest in chronic alcoholics—cerebral and cardiac arteriosclerosis, myocarditis, nephritis and liver degeneration. All in all, the proportion of patients who can be cured of their abnormal drinking behaviour by deterrent measures must be very small.

Gregory divides true curative measures into three categories based on the opinion that all forms of excessive drinking begin with a symptomatic stage—symptomatic of psychological or physical pathology or of bad social conditions. Patients at this stage are classified as "irregular symptomatic excessive drinkers"; sometimes this stage develops no further, but often these types become so dependent on alcohol as to come within the classification of "habitual symptomatic excessive drinkers". Further loss of control over the intake of alcohol leads to patients becoming "addictive drinkers", or alcohol addicts. The Alcoholism Subcommittee of the Expert Committee on Mental Health (W.H.O.) has defined "excessive drinking" as any form of drinking which in its extent goes beyond the traditional and customary "dietary" use, or the ordinary compliance with the social drinking customs of the whole community concerned. This is not a particularly useful definition—its range is wide and its limits are purely relative—but the subcommittee's definition of "alcoholism" is more specific and might well be studied by all connected with the problem of alcoholism: "Alcoholics are those excessive drinkers whose dependence upon alcohol has attained such a degree that it shows a noticeable mental disturbance or an interference with their bodily and mental health, their interpersonal relations and their smooth social and economic functioning; or who show the prodromal signs of such developments. They therefore require treatment." This definition covers both the habitual symptomatic excessive drinkers and the addictive drinkers. The approach to the cure of the basic causes of alcoholism, then, should be threefold. First, a careful search for any possible pathological cause must be made. Physical disease of one sort or another may aggravate an existing tendency towards alcoholism, and its treatment should help to alleviate the first stage at any rate. Further, some authorities have postulated that disturbances in certain physiological processes play a predominant part in the ætiology of alcoholism; especially has primary or secondary hypoadrenocorticism been blamed, and attempts have been made to restore normal balance by giving ACTH or cortisone; this work, however, is in the theoretical stage only. Second, and most important, is the search for a possible psychological basis for the condition. Here it is necessary to distinguish between cause and effect: metabolic changes caused by excessive drinking appear to play an important part in the development of such conditions as *delirium tremens*, acute alcoholic hallucinosis, Wernicke's encephalopathy and Korsakoff's syndrome; but it is agreed that a psychotic predisposition is a prerequisite when excessive drinking causes such conditions as chronic alcoholic hallucinosis or the alcoholic paranoid states—these are probably alcohol-stimulated manifestations of a hitherto latent schizophrenia. However, for the purpose of curing alcoholism it is necessary to investigate the psychological defects which let a particular patient develop into an excessive drinker. The commonest of these appear to be mental deficiency, psychopathic personality, psychoneurosis, schizoid personality, schizophrenia, "cycloid personality", hypomania and depression. Some of these may be relieved by electroconvulsive therapy, but verbal psychotherapy is the method usually employed, coupled with direct education of the patient's family and sometimes even of certain of his friends. It must be remembered, however, that the underlying personality defect of which the original irregular excessive drinking was a symptom, may have been aggravated or deviated later by the excessive drinking, or may have become overlain by acquired conflicts and confusions, so that even if it can be sorted out and treated, this will not affect the more

[1] *Canad. M. A. J.*, February 15, 1955.

severe stages of alcoholism which have subsequently developed, and which themselves may need special psychotherapy. Thirdly, there is social therapy. The most successful results appear to be obtained by a combination of psychological and social therapy. The organization known as Alcoholics Anonymous has a method of handling alcoholism which is a combination of applied group psychology and social rehabilitation, with a spiritual and inspirational approach; its efficacy is enhanced because its members are all former victims of alcoholism. Social therapy is contributory to the first two groups; its greatest use is in consolidating gains already made, by family and occupational rehabilitation. The other aspect of social therapy—the preventive aspect—is less attractive. Gregory states that education of the public is the most effective long-term preventive measure, but this is a vague prospect. In practice, the only really successful measure was the imposition by Denmark in 1916 of such a heavy tax on alcohol that few people were able to afford an excessive amount to enable them to indulge in excessive drinking; even this stratagem can be by-passed to a certain extent, but the alternatives of total prohibition or rationing have been proved failures.

To summarize, people like to, and will, drink alcohol, but many persons, because of basic defects, tend to drink excessively; this excessive drinking tends, in time, to become less symptomatic of the original basic defects and more pathological on its own account. There may sometimes be a physical basis for the tendency to drink excessively, and often defects in the social environment may be blamed, but usually the basis is in the lesser emotional disorders. The best time for curing excessive drinking is while it is still a symptom of these disorders. An important point is that the cooperation of the patient is always essential to the success of any treatment, but it is not always possible to convince the patient that there is a need for treatment; the first step in securing cooperation is to give him an insight into his state when drinking excessively. Alcohol's chief subjective effects are the relaxation of inhibitions, a feeling of exhilaration and the blotting out of memory—the hangover does not come till the morning. Nobody will believe that he did anything really bad or dangerous or disgusting while he was drunk—no amount of mere telling—nothing less than a few flashlight snapshots and a tape-recording will convince him. Full insight induced in such a way is capable alone of curing many patients in the early and less severe stages, and will ensure the cooperation of most of the others, so that thereafter attempts at treatment will have infinitely more chance of success. A second point is that the patient needs moral support at times of stress—his first need is a good, sound, plausible excuse for not drinking (for such are the times that to ask for lemonade instead of beer is a serious social solecism); his second, wide publicity of the right type, so that he dares not slide back lest his friends say "I told you so"; and his third, a loyal companion who will stand by and bolster up his determination whenever it wavers and give generous commendation when it remains firm. Alcoholism is certainly a condition requiring medical care, but adjuncts such as these are most desirable.

## A REPORT ON GASTROSCOPY.

ALTHOUGH gastroscopy has been a recognized diagnostic procedure for some years, its use has not become as general as might have been expected. This may be because too much has been expected of it—in other words its limitations, though known, have not been borne in mind—or because a good deal of experience is needed before expertness can be claimed and reliance placed on the findings. It should be recalled that gastroscopy became a safe procedure in 1932 when Rudolf Schindler and Georg Wolf introduced the flexible gastroscope which superseded those of a rigid type, the first of which was made by Mikulicz in 1881. Schindler published a book on the subject in 1937 and expressed the opinion that gastroscopy combined with X-ray examination could completely supplant exploratory laparotomy. There is no need to lay stress on the diagnostic value of X-ray examination in gastric conditions, but for the sake of completeness mention should be made of the method devised by Wood and others at the Walter and Eliza Hall Institute in Melbourne for the taking of biopsy specimens from the gastric mucosa. This was described in *The Lancet* of January 1, 1949. Wood and his co-workers suggested that their method might establish a histological diagnosis in a diffuse lesion of the stomach, and that it would be an adjunct to clinical and pathological study in many diseases in which the gastric lesion was not necessarily the chief feature. The three methods of investigation—gastroscopy, X-ray examination and the examination of biopsy specimens—have their own spheres of usefulness. In the present instance attention will be drawn to a fourteen-year survey of over 1000 examinations by gastroscopy.[1]

The report comes from John C. Meadows and Edward J. Lefeber, of the Department of Medicine at the University of Texas. Gastroscopy has been carried out as a diagnostic procedure at this department since 1940. During a fourteen year period ended 1953, 1076 examinations have been made. All examinations were made by one or more of three members of the staff of the department. There were no accidents attributable to the procedure. The initial examinations were made with the flexible gastroscope, later supplemented by the movable tip gastroscope, and later supplanted by the adjustable mirror gastroscope. The examiners were not impressed by any insignificant increase in the visible areas as a result of the use of the more elaborate instruments. The 1064 gastroscopies were carried out on 898 patients; there were 166 repeat examinations and 12 lost reports. Between 1940 and 1945 approximately 45% of the patients were examined because of their symptoms only; from 1946 onwards this percentage had been decreased to 25. All but three patients received some form of anæsthesia. Early in the series a combination of codeine and atropine was used as a general rule; this was later replaced by morphine and scopolamine; since 1945 meperidine has been used almost exclusively. In all cases local anæsthesia with 2% tetracaine hydrochloride was used. Intravenous anæsthesia, recommended by some authorities, was used in only seven instances. The gastroscopic diagnoses are set out in a circular graph. The finding was "normal" in 377 cases (33%); no diagnosis was made in 150 (13%). Chronic gastritis was diagnosed in 389 cases (34%); of these an atrophic form was present in 188 cases, a hypertrophic form in 144 cases, a superficial form in 58 and a mixed form in 29. Gastric carcinoma was found in 70 cases (6%) and benign gastric ulcer in 62 (5%). The diagnosis was "post-operative stomach" in 44 cases (4%), gastric polypi in 27 cases (2%) and "miscellaneous" in 35 cases (3%).

Rather than describe Meadows and Lefeber's findings in detail we must be content to set out some of their conclusions. They find that a gastroscopic diagnosis of an organic lesion can often be made among patients whose findings on X-ray examination are indefinite, and can occasionally be made in the case of patients whose X-ray appearances are normal. Organic lesions are seen more frequently at X-ray examination than at gastroscopy; at the same time they conclude that the gastroscopic diagnosis is more accurate than the radiological diagnosis. Organic lesions may be found at gastroscopy that are not visible on the X-ray picture. These statements are not contradictory, though they may appear to be. Chronic gastritis in the experience of these two authors is a frequent finding at gastroscopy and is particularly frequent in patients with duodenal ulcer. Meadows and Lefeber think that the assumption that chronic gastritis is the cause of otherwise unexplained gastro-intestinal bleeding may be fallacious. Gastric carcinoma may occur in patients with duodenal ulcer. The final statement is that gastroscopy appears to be indicated if a gastric lesion is noted at X-ray examination, if the X-ray findings are

[1] *Ann. Int. Med.*, January, 1955.

indefinite, or if the symptomatology is not in keeping with the radiological diagnosis.

This report by Meadows and Lefeber would seem to indicate that more attention should be given by clinicians to the use of the gastroscope. Those who wish to add to their diagnostic equipment by gastroscopy, however, will need to realize that the work is not simple, but that much patience and much time are needed in the mastery of the art. We may recall Schindler's insistence that an efficient gastroscopist must be not only a well-trained gastroenterologist, but also an expert technician and psychologist. Being an expert technician and psychologist, he will have to learn to interpret what he sees. Schindler's obvious statement may be repeated: "Merely owning a gastroscope does not make one a gastroscopist any more than the purchase of a scalpel qualifies one as a surgeon."

## ANTIBIOTIC THERAPY OF URINARY TUBERCULOSIS.

PREVIOUS REFERENCES have been made in these columns to some of the many reports of antibiotic therapy for urinary tuberculosis. However, a report by R. M. Nesbit and C. E. Mackinney[1] has certain individual features of interest. It is an interval report prepared after six years' experience. There were 90 patients in the series, and 53 of them had concurrent active tuberculosis outside the urinary tract, or gave a history of it. Of the 57 male patients in the series 44 had genital involvement of some kind. For most of the time the basic regimen consisted of two grammes per day of streptomycin or (latterly) dihydrostreptomycin. The antibiotics were used to augment rather than to supplant the well-established principles used in combating tuberculosis, and for this reason sanatorium care was used all through the antibiotic course and for six months afterwards. Para-aminosalicylic acid was also given by mouth in tablets to a dosage of 12 or even 15 grammes per day. Isoniazid was used as an addition to this regimen when a second course of therapy was necessary for relapse, or when patients failed to respond to the initial ninety days' course. In unilateral renal disease, when only small lesions were seen pyelographically, the above antibiotic therapy was given for sixty days, and then a check-up examination was made by full urological methods. If substantive improvement had not occurred, nephrectomy was performed and the antibiotic programme continued for another thirty days. In cases in which the initial urograms showed a moderate or advanced destructive process, nephrectomy was performed after only ten days' antibiotic therapy, and the antibiotic therapy was continued afterwards for ninety days. All patients had check X-ray examinations at three month intervals for the first year and every six months thereafter. Urine culture and animal inoculation studies were carried out monthly for the first year.

The results, for an interim report, are encouraging. Unilateral renal disease was treated in 42 patients; two-thirds of this group (28) had normal urine when last examined. In 21 of the unilateral cases nephrectomy was carried out as well as treatment with antibiotics, and 18 of the patients have remained well. In an equal number (21) of unilateral cases antibiotics only were used, and only 10 patients have remained well. As Nesbit and Mackinney state, the results of medical treatment alone certainly do not compare favourably with those of a combined regime in this group of cases. There were 30 cases in the bilateral group, and 23 of the patients have enjoyed remissions to date. Most of these patients had one kidney removed either prior to the antibiotic course or during it. Twelve patients in the group with bilateral disease did not undergo nephrectomy; in two-thirds of these patients the urine became normal, and it has remained so to date. Eighteen patients had normal kidneys, but had tuberculous bladders with or without genital involvement; 10 of these had had a previous nephrectomy, the remaining kidney still being apparently normal; 14 of the total group responded favourably to antibiotic therapy. The overall result in the whole group of 90 patients with uro-genital tuberculosis was that 65 had normal urine for six months to six years after the completion of therapy. Although most investigators today advocate a smaller dose of antibiotic given less often than in these studies, Nesbit and Mackinney intend to pursue their present plan of therapy in the hope that a comparison with reports of other series of patients treated with other programmes may eventually reveal just what plan of treatment is the best in yielding long-term good results. One point on which more information might be given in subsequent reports is the toxic effects of the antibiotics. The principal drug used in the studies has been dihydrostreptomycin; dismissal of its toxic effects in two sentences and a not very informative table is hard to accept when it is remembered that in many circles this drug has been abandoned altogether because of its toxicity.

[1] *J. Urol.*, September, 1954.

## THE AVOIDANCE OF SURGICAL PANIC.

WHEN a tornado crashed through Worcester, Massachusetts, on June 9, 1953, there were many surgical casualties urgently needing relief. Gashes from flying glass and sheet iron, bruises, fractures and internal injuries from falling masonry and timber were numerous and demanded quick attention.[1] Medical men, first-aid trainees and voluntary helpers worked heroically to treat the injured and place these when necessary in hospitals. When the emergency had receded, in time there came the realization that a state of panic had occasioned much faulty action; hospitals near the site of the tornado were overcrowded, whilst others quite accessible by motor ambulance or private car were almost empty; wounds were sutured though badly contaminated or even when foreign bodies were enclosed, this leading, as might be expected, to suppuration and subsequent unsightly scarring. Of course, in mitigation of the blame for this state of affairs, it should be noted that the disaster was totally unexpected and that no appropriate organization had previously been in existence. But the analysis of the conditions displays something more than the results of unpreparedness. In military medical science a well-thought-out plan of dealing with casualties has been evolved; there are facilities for transport, there are efficient communication systems, there are trained assistants, magazines of instruments, anæsthetics, antiseptics and drugs, and there are devices for good illumination; yet a rush of casualties from a battle has sometimes led to a regrettable confusion. Wilfrid Trotter, commenting on conditions in London in September and October, 1938, wrote: "In examining decisions reached under the influence of panic we are not to look for blunders and errors of judgement, for the fruits of ignorance or the fatuity of office, but for something at once more subtle and more characteristic. We are to look for decisions that could have been reached only by people in whom the faculty of practical reason was actually impaired . . . decisions which no normal mind in any circumstances could have assented to."[2]

Australia is fortunate in not having disasters attended by massive casualties. Flood and fire have brought about deaths which we all deplore, but the numbers of the injured have not overstrained hospital accommodation. Willy-willy and cyclone strike thinly populated areas. There are no earthquakes except harmless tremors. There remains the one hideous possibility of war in which the number of wounded in civilian life as in the services would reach astronomic proportions. Thus there is but one thing to do, to organize and reorganize, to rehearse and re-rehearse in mimic warfare, so that should what we

[1] *Ann. Surg.*, December, 1953; *Bull. Am. Coll. Surgeons*, January-February, 1955, page 21.

[2] *Brit. M. J.*, February 17, 1940; also in "The Collected Papers of Wilfrid Trotter", Oxford Medical Publications, Oxford University Press, 1946.

fervently hope will not be inflicted upon us actually take place, the horror of the situation will be somewhat attenuated by the perfection of preparedness.

## HYPOTHYROIDISM AND COBALT.

IN the issue of September 27, 1952, we discussed the use of cobalt in animal nutrition, mainly from the point of view of vitamin $B_{12}$. Vitamin $B_{12}$, an organic cobalt compound, is necessary for the formation of red blood corpuscles and hæmoglobin, and since its isolation it has been greatly used in the treatment of pernicious and other types of anæmia. It has been known for a long time that when cobalt is given in doses above certain amounts polycythæmia is produced in animals. During the past few years cobalt salts have been used in the treatment of types of anæmia in man not amenable to other forms of treatment including the use of vitamin $B_{12}$. Favourable responses have been claimed in sickle-cell anæmia and the anæmia associated with chronic infection and chronic renal insufficiency. In the doses of cobalt chloride used unfavourable symptoms are usually not severe and are due mainly to stomach irritation. This can be prevented by giving the cobalt in enteric-coated tablets. J. P. Kriss, W. H. Carnes and R. T. Gross have described[1] a more severe complication in five cases in which cobalt therapy was used during a period of several months. Four of the patients had sickle-cell anæmia and the fifth the anæmia associated with chronic renal insufficiency. Cobaltous chloride was given by mouth in enteric-coated tablets. Hyperplasia of the thyroid developed in all the cases after some months of treatment with cobaltous chloride. In three of the cases visible goitres appeared and in one case serious myxœdema developed. Tests of thyroid function, by radioactive iodine, showed marked depression of normal activity in the three cases tested.

H. C. Hopps, A. J. Stanley and A. M. Shideler have made histological studies[2] on the effect of cobalt salts in animals. Doses approximating ten times that recommended for human dosage for as long as thirty-two weeks were given to rats. No significant degenerative changes were found in the heart, lungs, liver, kidney, spleen, pancreas, salivary glands, testicle, epididymis and bone. Small changes were found in the spleen and considerable changes in the bone marrow consisting of hyperplasia affecting particularly the erythropoietic elements. All the animals developed polycythæmia. There is no evidence that the thyroid was examined, but in the human cases the thyroid hypoplasia was found only on histological examination in two of the cases. There is some evidence that cobalt inhibits certain enzymes concerned with oxidation. Cobalt inhibits the enzyme which catalyses the conversion of tyrosine to monoiodotyrine. If the evidence here presented is confirmed it will mean that cobalt is a goitrogenic agent and that the indiscriminate use of cobalt, especially in infants and children, should be avoided.

## THE TREATMENT OF "TENNIS ELBOW".

HYDROCORTISONE (17-hydroxycorticosterone, "Compound F") has effects as a parenteral rheumatic agent similar to those of cortisone; however, a suspension of the acetate salt is four times as active as cortisone, when injected locally. When it is used intraarticularly, early relapses occur and frequent injections are necessary. Now E. J. Crisp and P. Hume Kendall,[3] in "Hydrocortisone in Lesions of Soft Tissue", have followed up the suggestion that hydrocortisone acetate would be useful in lesions which are essentially reversible without any tendency to relapse, such as "tennis elbow" and "golfers' elbow", and various other soft tissue lesions in which trauma is followed by low-grade non-specific inflammation with local pain, tenderness and œdema, and the formation of adhesions with limitation of movement. Crisp and Kendall used a combined injection composed of 25 milligrammes of hydrocortisone acetate and 1000 units of hyaluronidase in two to five millilitres of 2% procaine hydrochloride solution. The procaine gives immediate relief from pain, and is accordingly an adequate guide to accurate localization, while the hyaluronidase ensures prompt local dispersion. The injection was given directly into the site of local tenderness, and the needle-point was moved about the site during injection; around the shoulder, if localization was not possible, the injection was given anteriorly into the subacromial bursa and laterally into the area of the long head of the biceps muscle, and occasionally into the region of the joint capsule, posteriorly. When there was acute effusion into a joint, without bony or discrete ligament injury, the procaine was omitted and the injection was made directly into the joint. No other treatment, active or supporting, was given; the injections were repeated at weekly intervals if necessary; if there was not considerable improvement after four weeks, the treatment was regarded as unsuccessful. Of 209 patients treated with a total of 350 injections, 133 obtained complete relief, 43 partial relief and 33 none, while 20 suffered relapses within three months of treatment; four of the failures and eight of the relapses were from 14 cases of bursitis, which responds only temporarily to hydrocortisone.

Lesions of the "tennis elbow" type are very disabling and annoyingly painful; although they ultimately respond to rest, after perhaps long periods of physiotherapy (of doubtful value), the total morbidity involved is out of all proportion to the nature and extent of the initial injuries; any method of treatment which will shorten the duration of the pain and incapacitation is most welcome. The small doses of hydrocortisone involved should be quite safe and should cause no anxiety.

[1] *J.A.M.A.*, January 8, 1955.
[2] *Am. J. Clin. Pathology*, December, 1954.
[3] *Lancet*, March 5, 1955.

## ABSTRACT ART AND AUTOSUGGESTION.

MANY people, braving the charge of philistinism, admit to being puzzled by what is known as abstract art—or rather by the fact that other people take it seriously. This especially applies to the three-dimensional creations just now fashionable, which are summed up by Sir Henry Turner[1] as "holes, knobs and wires" and have been a godsend to *Punch* artists. Attempting to explain the phenomenon, Turner suggests an experiment:

> Take three (or more) upholsterer's coiled springs, entangle them, and mount the result in an inverted aquarium bowl indirectly lit, with a professionally lettered card reading (for example) *Time Passing*. This should be exhibited in a place of some importance. Failing the Tate, a Bond-street art-dealer's window will do.

Four types of reaction are expected: (*a*) confident, extravert derision; (*b*) open disconcertment ("I suppose I ought to see something in it"); (*c*) insincere praise; (*d*) prolonged study, and a true statement of pleasure in a new æsthetic experience. Turner is not worried about those in class (*a*)—"they are happy enough"; but he is concerned for the uncomfortable inferiority feeling associated with (*b*) and the "unpleasant, self-damaging deceitfulness" indicated by (*c*). He regards those in class (*d*) as the prime instigators of the confusion and suggests that their reaction depends on auto-hypnosis. Without dogmatism he develops this hypothesis and submits it for consideration. There seems indeed to be something in it, particularly in view of the tendency of hypnotic suggestions to wear out; abstract art cults succeed one another with bewildering rapidity in contrast to the enduring appeal of more straightforward styles. Escapism may, of course, be involved, but it is not always to be despised.

[1] *Lancet*, April 9, 1955.

# Abstracts from Medical Literature.

## DERMATOLOGY.

### Allergic Sensitization of the Skin and Oral Mucosa to Acrylic Denture Materials.

A. A. FISHER (*J.A.M.A.*, September 18, 1954) states that a review of available reports shows that reactions to acrylic denture materials may be divided into (i) an allergic, eczematous, contact type of dermatitis affecting dentists and dental mechanics and (ii) allergic stomatitis affecting wearers of dentures. Four patients were studied who had an allergic contact type of dermatitis of the hands that was proved clinically and by patch testing to be due to allergic sensitization to the liquid monomer (methyl methacrylate). These patients were not allergic to polymethyl methacrylate powder or to heat-cured denture material. Two of the patients could wear acrylic dentures in spite of the fact that they were sensitive to the monomer. They were also sensitive to patch testing to denture material made with self-curing monomer, showing that with this material there is sufficient unpolymerized monomer that can produce reactions. Methyl methacrylate liquid monomer is a sensitizer and can cause an allergic contact type of eczematous reaction on the skin and the oral mucous membranes. When it is completely polymerized, it is no longer a sensitizer or eliciter of allergic reactions. No instance of allergic sensitization to heat-cured acrylic denture material was found. As shown by controls, many persons will react to the strapping of any type of denture on their arms with redness, papulation or even bulla formation. This appears to be a non-specific pressure effect.

### Erythromycin in Treatment of Dermatoses.

H. M. ROBINSON, I. ZELIGMAN, R. C. V. ROBINSON, M. M. COHEN AND A. SHAPIRO (*Arch. Dermat. & Syph.*, September, 1954) state that erythromycin is an antibiotic substance produced by an actinomycete which has been identified as a strain of *Streptomyces erythreus* on the basis of cultural characteristics, physiology and microscopic morphology. They record observations on 1695 patients with various dermatoses who were treated with erythromycin; 681 received the drug by mouth and 1014 by local application of 1% ointment. For administration by mouth, special enteric-coated tablets of 100 milligrammes and 200 milligrammes were used. The following ointment for local application was used: erythromycin 1·0 part, heavy mineral oil 5·0 parts, petrolatum 94·0 parts. Erythromycin tablets proved to be of benefit when given by mouth in the treatment of all conditions in which pyogenic organisms were the primary cause of the disease. They were also of value for secondary pyogenic infection of atopic dermatitis, epidermophytosis and seborrhœic dermatitis, but had no beneficial effect on the patients in relation to the primary disease. Rapid involution of the lesions of *granuloma inguinale* occurred after erythromycin therapy. The drug was also of value in cases of *erythema multiforme*. No blood dyscrasias occurred. Erythromycin ointment caused rapid healing of pyogenic infections such as *impetigo contagiosa* and ecthyma. It was also of value in the treatment of dermatoses with secondary pyogenic infection, but not of value in the primary condition. The authors emphasize that the drug should be used only when there is a specific indication.

### Juvenile Melanoma and Malignant Melanoma in Children.

H. E. MCWHORTER AND L. B. WOOLNER (*J.A.M.A.*, October 16, 1954) state that the juvenile melanoma is a newly identified lesion that appears to be benign and can be differentiated histologically from malignant melanoma with which it has been confused in the past. It can be treated by complete removal, which need not be radically wide. Malignant melanoma occurs in children and may result in metastatic spread and death. It is rare in pre-pubertal persons. Suspicion should be aroused, in children as in adults, by any rapidly growing, easily traumatized or ulcerated growth, or by one that is darkly pigmented or that has changed in colour. The generally accepted treatment for the local lesion of malignant melanoma is that of radically wide excision with the probable need of a skin graft. Radical dissection of the regional lymph glands is indicated whenever palpable and operable nodes are present. The patient should be checked frequently for any evidence of involvement of lymph glands. Routine dissection of regional glands as a "prophylactic" procedure is not, according to the authors, warranted on the basis of present evidence.

### The Cutaneous Manifestations of Polyarteritis Nodosa.

H. LEYELL AND R. CHURCH (*Brit. J. Dermat.*, October, 1954) state that the acute stage of *polyarteritis nodosa* is accompanied by polymorphic exanthemata, but the more characteristic manifestations reflect vascular damage present. Nodules in the skin and subcutaneous tissues were described in the original cases of 1866. The picture then presented of an acute febrile illness with pallor, weakness and extreme muscle pains, colic, paræsthesia, tachycardia, hæmaturia *et cetera*, with a short course ending always in death, remained the whole conception of the disease for many decades. Of recent years, many cases confirmed by biopsy of a subcutaneous nodule have been shown to end with the patient's recovery. When nodules are present, they may number up to fifty and show a tendency to grouping and varying in size from that of a pea to a hazel nut. The nodules may regress in a few days or persist for eighteen months. The lesions are sometimes painful and tender. The overlying skin may be unchanged, reddened or thinned and glistening, or it may ulcerate. Ecchymosis and gangrene resulting from rupture of an aneurysm or weakened arterial wall are characteristic. Gangrene of the extremities has been described. In the chronic stage, affection of peripheral vessels may give rise to Raynaud's phenomenon, and dry gangrene may develop in the extremities. The acute stage of *polyarteritis nodosa* is accompanied by various exanthemata, of which purpura is the commonest. A papulo-bullous rash with ulceration of the mouth was present in an acute case recorded by Debré. Urticaria is described in the acute stage, but is usually accompanied or succeeded by a hæmorrhagic eruption. The relationship of *polyarteritis nodosa* to a streptococcal infection has frequently been noticed. Œdema is present in about half the recorded cases of *polyarteritis nodosa*. *Livido reticularis* occurs in some normal subjects as a transient phenomenon on exposure to cold. Persistent reticular livido was first described in association with *polyarteritis nodosa* in 1935. *Livido reticularis* usually occurs in the chronic stage. Ulceration and *livido reticularis* may occur. The ulcers develop in a similar way to those in cases of acute skin gangrene, commencing as violet areas of discoloration, many of which become necrotic and ulcerated. The skin is involved in about a quarter of cases of *polyarteritis nodosa*.

### Treatment of Dermatitis Repens with Peruvian Balsam.

R. S. BLOOM AND A. L. LORINCZ (*Arch. Dermat. & Syph.*, December, 1954) report three cases of *dermatitis repens* because of the rapid and striking therapeutic results obtained in each case with 10% Peruvian balsam in petrolatum after many previous attempts at therapy had failed. They state that the entity of *dermatitis repens* is rather poorly defined. Its differential diagnosis includes *acrodermatitis continua* of Hallopeau, pustular psoriasis, *acrodermatitis pustulosa perstans* of Sachs and pustular bacterid of Andrews. Culture of the purulent exudate on several occasions revealed *Pseudomonas aeruginosa, Streptococcus fæcalis*, β hæmolytic streptococcus, *Escherichia intermedius* and *Paracolobactrum aerogenoides*. The in-vitro antibiotic sensitivities of these organisms were tested. However, treatment with the antibiotics to which most of these organisms were sensitive failed to be effective clinically. In one case *Pseudomonas aeruginosa* was completely resistant to all ten of the antibiotics the authors had available for testing. The authors studied the antibacterial effect of Peruvian balsam on antibiotic-resistant organisms by using various concentrations of the agent emulsified in brain-veal-agar culture medium. A relatively high concentration of the agent was necessary for complete inhibition of bacterial growth.

### Observations on Porphyria Cutanea Tarda.

L. S. BRUNSTING (*Arch. Dermat. & Syph.*, November, 1954) states that in *porphyria cutanea tarda*, that is, the purely cutaneous type of porphyria, the onset is at middle age or later, and the course is mild but persistent. Hepatotoxic factors are prominent, and functional impairment of the liver is common. The blistering skin reaction is often explosive and directly related to exposure to the sun. Attacks of abdominal or nervous symptoms coincide or alternate with the cutaneous phase or smoulder in the background. The characteristic features are low-grade blistering and an erosive tendency on light-exposed surfaces of the skin, with melanosis and violaceous hue. Hypertrichosis was observed in seven women. Hyperpigmentation was common and was a diffuse process or mottled; sometimes it was associated with vitiligo of the hands. Sclerodermoid yellowing and hardening of

the exposed skin of the face and back of the neck were of common occurrence. In a few instances, punched-out craters and healed scars were observed about the cheeks and back of the neck. Blistering was an irregular feature, occurring mostly in the fingers and hands. As a rule, patients with *porphyria cutanea tarda* excrete large amounts of pre-formed porphyrins in the urine and fæces, and no porphobilinogen. The urine usually contains uroporphyrin and coproporphyrin; the fæces contain uroporphyrin, coproporphyrin and, sometimes predominantly, protoporphyrin. As regards treatment, avoidance of exposure to sunlight is helpful, but most important is elimination of the damaging insult to the liver by the strict avoidance of alcohol or hepatotoxic drugs.

### Interdigital Pilonidal Sinus.

H. L. JOSEPH AND H. GIFFORD (*Arch. Dermat. & Syph.*, November, 1954) state that the clinical appearance of barber's interdigital pilonidal sinus is that of a small symptomless opening on the dorsum of the interdigital web. It is often tiny, barely visible to the unaided eye and appears as a small black dot owing to the short hairs which protrude or can be expressed. The authors have found no opening over one millimetre in diameter. When the affected web is picked up between the examiner's fingers, a small cyst-like nodule can be palpated in the skin over the opening. Interdigital pilonidal sinus is an occupational disease amongst barbers due to extraneous short hairs which penetrate the skin and act as foreign bodies. The condition is usually benign, but occasionally becomes disabling, as is shown in the authors' case in which the patient developed six lesions in four interspaces complicated by repeated infection and recurrence in surgical scars.

## UROLOGY.

### Necrotizing Renal Papillitis.

B. WALL (*J. Urol.*, July, 1954) states that characteristic pyelographic changes occur in papillary necrosis in the kidney. These changes may simulate those of renal tuberculosis, but differ from the changes due to chronic pyelonephritis. The author reports three cases with definite pyelographic appearances; two of these occurred in association with diabetes, which seems to be the commonest underlying factor; in the other case the ætiology was not clear. There is a possibility that *periarteritis nodosa* due to sulphonamide reaction can be a cause. Strict aseptic technique should be followed in the instrumentation of diabetics; diabetic urine is a fertile culture medium.

### Interstitial Cystitis in Males.

W. J. BAKER AND E. C. GRAF (*J. Urol.*, October, 1954) state that the post-operative course of patients who have had endoscopic prostatic resection is occasionally complicated by persistence of vesical irritability. Usually the cause of this is incomplete resection of prostatic tissue, a necrotic residue of prostatic tissue, a persistent infection which delays epithelialization, strictures of the urethra or infection of the male internal genitals. The authors report a group of cases in seven male patients. In these none of the usual causes operated. They were all found to have definite interstitial cystitis; this was of the usual primary type described by Hunner, and was probably present before the prostatic lesion was resected. The authors state that interstitial cystitis affects all coats of the bladder and is also called panmural cystitis. This inflammation is patchy in nature and usually affects the dome of the organ. It is not associated with infection of the urine, but is characterized by day and night frequency of urination, marked urgency and severe suprapubic pain when the bladder is distended. Over-distension of the bladder during cystoscopy produces visible cracks or bleeding ulcers, disposed in a linear fashion. Other parts of the organ are entirely normal. In the seven cases reported, all patients were in the "prostatic" age-group. Endoscopic resection of small obstructions was performed, but did not relieve the irritability symptoms; these persisted until the interstitial cystitis was observed and diagnosed, and then treated by over-distension, diathermy and so on, when relief was obtained.

### Renal Papillary Necrosis.

R. A. GARRETT, M. S. NORISS AND F. VELLIOS (*J. Urol.*, October, 1954) state that the scarcity of reports in urological literature about papillary necrosis of the kidney has prompted submission of this report on six cases observed since 1945. The disease is a serious one; four of the six patients in this series are dead, and two survive (early 1954). One hundred and sixty cases have been recorded in the literature since 1877. Ninety-six of these cases occurred in diabetics, and diabetic females suffered from the disease twice as often as males. In the non-diabetic cases male subjects were predominant (six to one), probably because urinary tract obstruction has a far greater incidence in men. Practically all patients with this disease have either *diabetes mellitus* or urinary tract obstruction. The majority of patients are over fifty years of age. The lesion was bilateral in 61 out of the 160 cases in the literature. Renal papillary necrosis must be suspected in any diabetic with severe acute pyelonephritis, gross hæmaturia, renal colic, micturition of solid material or rapidly progressive renal insufficiency not responsive to chemotherapy and diabetic management. The disease may be an acute, fulminating, rapidly fatal process, or it may be relatively chronic and progressive, with or without acute and severe episodes. Oliguria and anuria may occur. The severity of the diabetes does not seem to be a factor. Gross hæmaturia may denote sloughing of a papilla. Renal colic indicates obstruction of an infundibulum or ureter by the sloughed parenchyma. The passage of actual papilla in the urine is, of course, a dramatic event. This is, however, seldom observed, since such masses are either overlooked or undergo liquefaction. Retrograde pyelography is often very helpful; early changes show ragged calyceal outlines reminiscent of tuberculous lesions. Later, if a papilla sloughs away, a diagnostic "ring-shadow" is left in the position of the calyx, and a filling defect in the renal fibres indicates the presence of the sloughed papilla. Such a pathognomonic picture is, however, rare. In the ætiology, the factors in necrotizing papillitis are thrombosis or compression of vessels supplying the renal pyramids. The necrosis may affect a whole papilla, or only a part thereof. The necrotic zone, with later line of cleavage, works from the edges towards the centre of the papillary base. In the management, infection is the dominating matter; sensitivities of offending organisms must be tested, and potent antibiotic therapy must be instituted rapidly. No urinary obstruction factor must be allowed to continue; and if ureteric catheter drainage does not bring improvement, surgical drainage must be effected. Nephrectomy has been advocated and may be life-saving. However, careful consideration of the medical management, exclusion of the existence of bilateral disease and evaluation of total renal function must precede any radical decisions. Of the authors' six patients, all were diabetics except one. The diagnosis of acute pyelonephritis was made in all cases, and bacteriæmia was present in three. Two of the four patients studied at autopsy had intercapillary glomerulosclerosis. Bilateral papillary necrosis was found in three cases.

### Neoplasms of the Testis.

G. T. THOMAS AND A. J. BISCHOFF (*J. Urol.*, September, 1954) have made an analysis of 80 cases of testicular tumour recorded between 1946 and 1950. The conclusions reached are summarized in the following statements. It is unlikely that trauma *per se* is an ætiological factor in malignant neoplasms of the testis. The relation of cryptorchidism is more than coincidental; ten of the 80 malignant lesions occurred in undescended testes, and in three of the ten cases an orchidopexy had been performed previously. A hard, heavy, non-transilluminating, unilateral scrotal mass in a young adult is presumptive evidence of neoplasm, though men in older age groups are not exempt. Vague abdominal symptoms or cervical masses in a young patient may point to a testicular tumour, and a very careful examination is obligatory. Symptoms of obstruction of the upper part of the urinary tract, particularly if unilateral, may stem from a tumour of the testis; careful inspection and palpation of the external genitalia can be of major importance. Results of hormonal assays of the urine by various methods were encouraging as diagnostic aids; the serofloccculation test had a 90% accuracy. Palpable abnormalities of the genitalia may be absent even though biopsy of extratesticular masses may indict the testis. If a unilateral scrotal mass is present, exploration should be carried out without delay, for this is a better choice than missing a testicular cancer by conservatism or procrastination. About 95% of testicular tumours are malignant. Seminomata metastasize slowly but more widely than other testicular tumours. Despite its reputation for a lower degree of malignancy, a seminoma should be treated just as radically as other testicular tumours. Delay in seeking medical advice and delay in proceeding to operation are extremely hazardous. The lapse of time between onset of symptoms and operation was six months (average) in the group of treated patients who were still alive when this report was prepared, whereas the lapse in patients who had died averaged eleven months.

# Special Article.

## THE SALK POLIOMYELITIS VACCINE.

(CONTRIBUTED BY REQUEST.)

No detailed account of the results obtained in the American tests of the Salk poliomyelitis vaccine has yet been made available to Australian readers. We can, however, assume from what has appeared in the Press that in the vaccinated group there were only 10% to 15% of the number of diagnosable poliomyelitis cases which occurred in a comparable unvaccinated group. It is reported that deaths from poliomyelitis showed a similar ratio—11 in the control group, one in the vaccinated series.

These results were from a carefully controlled experiment of a magnitude exceeding anything of the sort previously attempted. Approximately 450,000 children were included in each group. The control children received an inert inoculum similar in nature to the vaccine, but derived from uninfected tissue cultures. The inocula were labelled in code, and neither the child nor the person administering the vaccine knew whether vaccine or blank inoculum was being used.

The workers in charge of the test can be relied on to have taken every precaution to ensure that the result is a fully valid indication of the worth of the Salk vaccine as judged not by antibody production, but directly by its power to prevent symptomatic poliomyelitis and death.

This article is an attempt to summarize the implications of these results for Australia.

1. The vaccine used in the American tests was prepared by growing three strains of poliomyelitis virus, one of each serological type, in tissue cultures of monkey kidney. When a satisfactory concentration of virus was obtained, the culture was killed by formalin, filtered and tested for sterility and immunizing capacity. Elaborate technical control of all these steps was, of course, necessary.

2. The test vaccine was prepared according to a standardized procedure by a number of commercial drug houses and checked by an official organization.

3. The results obtained are strictly speaking applicable only to the vaccine prepared and used in 1954. They can, however, be legitimately extended to cover all vaccines made by the Salk procedure which have an equal or better content of virus antigen and which have satisfied the test requirements for sterility and antigenic power.

4. In view of the fact that any test of a new poliomyelitis vaccine would have to be made on a similar scale involving millions of pounds' expense if it was to provide a definite assessment, we can feel certain that for at least five years the Salk vaccine or minor improvements thereof will be the standard agent for the prevention of poliomyelitis.

5. The 1954 results show that effective immunity lasts for some months. The problem of prolonged or permanent immunity has not yet been clearly visualized. Policy will have to be determined very largely by what influence large-scale immunization has on the invisible spread of poliomyelitis viruses through the community. One might hazard a guess that the definitive recommendation might be (*a*) a primary course of two injections spaced six weeks apart between six and twelve months of age, (*b*) a single (booster) injection in the spring of the following year, and (*c*) a second booster injection at the time of entering primary school.

6. Public interest in poliomyelitis is so acute that one must envisage from the start a policy of universal immunization. With an Australian birth rate of approximately 200,000 *per annum*, this would require an annual production of 800,000 doses; and if the objective was to protect all children from one to eleven years of age as soon as possible, an additional 6,000,000 doses, presumably spread over several years, would be needed.

7. To produce 2,000,000 doses *per annum* will require a moderately large capital expenditure for laboratories *et cetera* and a very high annual cost mainly for skilled technical work of perhaps £2,000,000 to £5,000,000. Probably 1000 to 2000 monkeys will need to be imported annually. It may become necessary to establish breeding colonies of Rhesus or other suitable monkeys in Australia.

8. It is clear that the adoption of universal immunization with the Salk vaccine will be expensive and will represent a considerable drain on skilled manpower.

9. The Salk vaccine made according to specification is safe and effective. Any relaxation in technical control would make it possible (*a*) that live virus in the vaccine will produce paralytic infection in some of those inoculated, or (*b*) that the vaccine will be deficient in antigen and hence in immunizing potency. History suggests also that unexpected and unforeseeable accidents may occur when an agent like this is used on a nearly universal scale.

10. There is an important body of opinion amongst American virologists which holds that the Salk vaccine is a temporary expedient and that effective and long-lasting immunization will eventually be better obtained by the use of an appropriate series of living virus vaccines given by mouth. No proved means of doing this is as yet available.

F. M. BURNET,
Melbourne.

# British Medical Association News.

## SCIENTIFIC.

A MEETING of the Victorian Branch of the British Medical Association was held at the Latrobe Valley Community Hospital, Yallourn, Victoria, on July 31, 1954. The meeting took the form of a series of clinical demonstrations by members of the medical and surgical staffs of the hospital.

### Primary Sarcoma of the Ovary in an Infant.

DR. L. GANZ presented a female child, aged two years, who had been admitted to hospital on November 9, 1953, suffering from severe abdominal pain and vomiting of twenty-four hours' duration. It was stated that she had always been a healthy child, and the mother had never noticed an abdominal swelling. On admission of the child to hospital, her abdomen was greatly distended and very tender, and generalized rigidity of the abdominal wall was present. A tender swelling was felt *per rectum*, and therefore a pre-operative diagnosis was made of generalized peritonitis caused probably by a perforated appendix. At laparotomy a solid tumour was found originating in the left ovary and filling the whole pelvis. It was gangrenous, the pedicle being twisted four times anticlockwise. Free fluid was present in the abdomen. The uterus and right adnexa were normal, and no secondary deposits were found. A left salpingo-oophorectomy was performed. The whole tumour was examined at the Women's Hospital, Melbourne, and the histopathological appearances were regarded as being rather typical of a sarcoma of the ovary. The patient was discharged from hospital on the fifteenth day after operation. No post-operative irradiation was carried out, this course having been decided upon after consultation with the Peter McCallum Clinic. Dr. Ganz said that at present the child was doing well and putting on weight. She had developed normally and there was no evidence of recurrence. From a perusal of the world literature the patient appeared to be one of the youngest sufferers from primary sarcoma of the ovary amongst the cases on record.

In further discussion of the case, Dr. Ganz outlined the difficulty in diagnosis, especially that involved in the exclusion of pneumonia. The breathing was rapid, and the chest was not quite clear clinically. Pneumococcal peritonitis had been considered likely. Further, diagnosis of the nature of the tumour found at operation was difficult. Dr. Ganz regarded it as a teratoma and was surprised at the histopathological report of sarcoma. Two months after operation the right inguinal glands had become enlarged, but subsequently they had subsided. Dr. Ganz thought that the prognosis was reasonable in view of the good subsequent progress that the child had made.

DR. F. D. STEPHENS congratulated Dr. Ganz on the successful outcome of the case. He said that he could not recall any solid tumours of the ovary removed by operation at the Royal Children's Hospital. He quoted three cases of large cysts in young children, which were the only ones with which he had been associated. One was a mesenteric cyst, another was a malignant tumour situated at the bifurcation of the aorta (that tumour recurred, although irradiation had been carried out), and the third was a hydatid cyst of the pouch of Douglas.

DR. G. WEIGALL asked if anyone present had had experience of the results of complete extirpation of sarcomata in young children.

DR. J. MCLEAN remarked on the microscopic appearance of the cells, which showed branching processes like a reticulosis. In view of that finding he felt that the prognosis might be more hopeful.

DR. J. PETERS was pessimistic about the outcome, especially in view of the post-operative treatment. However, he was of the opinion that nothing further should be done.

### Compound Depressed Fracture of Skull with Multiple Fractures of Extremities.

Dr. Ganz's second patient was a man, aged twenty-two years, who had been admitted to hospital on May 22, 1954, with multiple injuries resulting from a fall from a height of approximately 30 feet. He was fully conscious on admission to hospital and complained only of pain in both wrists and the right foot. Examination of the patient revealed a linear laceration of the scalp five inches long, extending from the right side of the forehead upwards, in which there was pulped brain matter. In addition, he had a compound comminuted fracture of the right forearm with radial paralysis, a comminuted fracture of the left forearm and a comminuted fracture of the right *os calcis* and the mid-tarsal bones.

First, the head injury was attended to under local anæsthesia. The laceration was excised and sutured, and a right frontal flap was raised. The contaminated bony fragments were removed, one fragment of about one square inch being found buried in the frontal lobe of the brain. Hæmostasis was secured, all lacerated brain tissue was removed by suction, the dura was closed, and the wound was closed without drainage. Two days later, the fractures of the forearms were reduced under local anæsthesia and immobilized. A fortnight later a subtaloid and mid-tarsal arthrodesis was performed on the right foot. After operation, the patient developed euphoria. Dr. Ganz said that the patient still, at the present time, had radial paralysis, which probably would have to be rectified by multiple tendon transplants. Loss of sensation in the fingers of the left hand was gradually becoming less. The right foot was painless. The defect in the skull would be repaired, either by a bone graft or by a tantalum plate. The patient could now walk reasonably well, and the foot was painless. There was severe limitation of function of the right upper limb. Dr. Ganz considered that arthrodesis of the foot gave the best results. The outlook for recovery of the right radial nerve was poor because of the sepsis present and because of the large amount of nerve torn by the injury. Dr. Ganz remarked in passing on the frequency with which patients who had had accidents in Yallourn had wounds contaminated with briquette dust, and on how difficult that was to remove.

DR. K. HALLAM quoted the school of thought that stated that many patients with a fractured *os calcis* also had fractured lumbar vertebræ. He asked whether spinal fractures were frequent at Yallourn.

In reply, Dr. Ganz said that he had had no patient with both fractures at Yallourn.

DR. J. M. ANDREW quoted one case that had occurred in his memory.

DR. WILSON thought that the wrist fracture should have been attended to early in spite of the poor general condition of the patient. He said that in that way severe complications might have been offset. He considered that transplant of flexor muscles to extensor tendons would be unsuccessful, and that arthrodesis of the wrist with reeducation of the remaining extensor muscles would be the best treatment.

DR. FITZPATRICK asked at what site the radial nerve had been injured, and also whether the briquette dust was highly infective material.

In reply, Dr. Ganz said that he knew of only one case of gas gangrene that had occurred at Yallourn, but he found contaminated wounds difficult to keep surgically clean.

DR. ROWAN WEBB defended Dr. Ganz's management in treating the head first, the hands second and the foot last. He recommended that at least immediate cleansing should be carried out with skin closure of wounds; that would prevent infection becoming established. He indicated how successful that procedure had been in military practice.

### Valvular Disease.

DR. J. JOSEPHS presented a man, aged thirty-five years, who had had a long history of doubtful "lung and heart trouble". He was said to have had "fracture of the windpipe" at the age of eight years with severe pneumonia at that time. Since then he had had dyspnœa and noticed gasping when he went up hills or exerted himself. Whilst under treatment for ulnar bursitis in May, 1954, the patient had developed acute heart failure with auricular fibrillation, which was controlled with digitalis and thiomerin. Dr. Josephs said that the patient had been referred to Dr. M. Davis, at the Alfred Hospital, who considered that the right ventricle and conus were enlarged, the condition suggesting pulmonary hypertension. Further investigations were carried out, and it was thought that thoracotomy was indicated. Soon afterwards the patient developed congestive failure and fibrillation.

DR. H. B. KAY reported that the left auricle was small and regarded the patient as suffering from mitral stenosis with incompetence. He felt that thoracotomy would be indicated if he failed to improve.

DR. L. HURLEY felt that there was little doubt about the diagnosis. He enumerated the physical signs as typical. He commented on the peculiar shape of the finger nails, which were rounded and bulbous, and according to the patient had always been so. Dr. Hurley said that he believed that there was no clubbing present, but wondered if bacterial endocarditis could have followed the ulnar bursitis. The question of surgical treatment depended on the result of the investigations. He felt that the condition was mainly one of stenosis.

DR. H. WILSON considered that there was little evidence of paroxysmal dyspnœa, but that the patient's dyspnœa was due to pulmonary congestion, and that he was changing over from a state of compensated to one of decompensated pulmonary hypertension. That would be evident radiologically as congestion of the proximal lung fields rather than of the peripheral fields. Dr. Wilson was of the opinion that the lesion was mainly regurgitant in view of the pronounced systolic murmur present. He believed that the patient's condition had gone on to one of functional tricuspid incompetence, but that this was not great because of the minimal liver enlargement. He himself would not operate on the patient; he would not embark on a forlorn hope. All patients said that they were better after exploratory thoracotomy, even if nothing was done. Possibly opening the pericardium was responsible for that, as was evident from the improved performance of greyhounds who were subjected to the operation.

### Migraine.

DR. V. W. O'KEEFE presented a married woman, aged thirty years, who after the menarche, at the age of fourteen years, had had two or three attacks consisting of left homonymous hemianopia followed by anæsthesia of the left hand and accompanied by a feeling of "remoteness", again followed by generalized headache lasting from one to two days. At the age of fifteen years the patient suffered from poliomyelitis. During her first pregnancy she had five similar attacks, in one of which speech was disordered. Her second pregnancy was quite normal (she was confined in December, 1952). In March, 1953, she suffered from slight diplopia for two or three days without visible squint. At her third pregnancy her last menstrual period was on September 3, 1953. On November 18, 1953, she had a severe attack with hemianopia lasting for two or three hours, anæsthesia of the left forearm, left hand and left side of face and tongue, with dysphasia, and severe headache lasting for three days. After that attack, she developed ptosis of the left eyelid, which was worse in the evening than in the morning. She was admitted to the Royal Melbourne Hospital on November 25, 1953. Lumbar puncture revealed no abnormality. An angiogram of the right carotid artery also revealed no abnormality, but the injection was followed by anæsthesia of the left hand and scintillating scotoma. An electrocardiogram showed no abnormality. Attempted angiography of the right vertebral artery was unsuccessful. The patient was discharged from hospital on December 11, 1953. The ptosis had become less during her stay in hospital, but it returned after she was discharged from hospital. It again began to lessen in March, 1954, but at that time she noticed diplopia on looking down. About the same time she had a severe attack of migraine relieved by the administration of a one-milligramme tablet of ergotamine tartrate. In May, 1954, the first attack occurred in which the effects were referred to the right side. Further attacks occurred on the right and left side until the patient was confined in June, 1954, since when she had had very slight ptosis and diplopia.

Commenting on the case, Dr. O'Keefe said that he felt that a likely diagnosis was an aneurysm of the circle of Willis with repeated small leaks, but the findings of angiography excluded that. He thought that the ptosis was a passing feature.

Dr. G. Weigall contended that the patient's condition conformed readily to a diagnosis of migraine. He said that to be typical the attacks should present an aura, the hemicrania should not be localized to one side, vomiting should usually be a feature, and prostration should occur after the attack. He was of the opinion that the persistance of left-sided phenomena in the early attacks was suspicious, but they had become more characteristic later when right-sided features appeared.

Dr. K. Liddett said that on examination of the patient he had found left ptosis and inferior rectus palsy, which was shown by the presence of diplopia when the patient looked downward. He discounted the idea that the ptosis was the result of the poliomyelitis. He said that the treatment was difficult, but he had found that many such patients had a refractive error, and some were relieved by the correction of that error. He believed that small doses of phenobarbitone (for example, one-quarter grain three times a day) given for months provided most relief to the largest number of patients. Although ergotamine tartrate relieved many, it made many very ill.

Dr. Spring asked whether vitamin $B_{12}$ therapy was effective.

Another speaker reported success with antihistaminics.

Dr. Weigall said that he believed that the sedative effect of the drugs was probably responsible for their success. The patient affected with migraine was usually a "top-gear personality", and sedation was very useful. He recommended the use of ergotamine first as an injection. The patient, knowing that an effective means of treatment was available, was more likely to respond subsequently to tablets of ergotamine.

### Leuchæmia.

Dr. O'Keefe then presented a boy, aged six years, suffering from leuchæmia. In 1948 he had had convulsions. In 1949 he had had tonsillitis and was treated with sulphonamides. In 1951 he had had cervical adenitis and again was treated with sulphonamides. In January, 1953, he suffered from an attack of an upper respiratory tract infection and was treated with sulphonamides, followed two days later by granulocytopenia and anæmia, which was treated with penicillin, "Pentnucleotide", pyridimin and blood transfusion. He was discharged from hospital in February, 1953, with a hæmoglobin value of 78% and a leucocyte count of 4000 per cubic millimetre. He remained well until May, 1953, when he developed a sore throat with enlargement of the cervical glands, splenomegaly and pallor. His hæmoglobin value was 62%, and his leucocyte count was 10,000 per cubic millimetre with 9% of blast cells. On May 26 his hæmoglobin value was 65%, his total erythrocyte count was 3,000,000 per cubic millimetre, and his leucocyte count was 7000 per cubic millimetre. The red cells were well stained. There was a moderate degree of anisocytosis and poikilocytosis. An occasional normoblast was seen. Platelets were present, but in a reduced number. The differential white cell count showed metamyelocytes 1%, band neutrophile cells 4%, neutrophile cells 8, eosinophile cells 1%, basophile cells 2%, lymphocytes 50%, monocytes 4% and "blasts" 30%. Examination of a bone marrow film showed that it was very cellular. A differential count revealed the following proportions: myelocytes 0·5%, band neutrophile cells 2%, lymphocytes 2·5%, pronormoblasts 0·5%, normoblasts 9%, reticulum cells 9·5% and "blasts" 76%. The pathologist, Dr. McLean, reported that the diagnosis from the tests was acute leuchæmia, possibly of the reticulum cell type. The patient was treated with "Aminopterin" 0·5 milligramme daily, blood transfusion and "Aureomycin" 100 milligrammes four times a day (the latter because of intractable bronchitis). "Aureomycin" therapy was ceased after one month, and the course was repeated twice for upper respiratory tract infections. The blood picture then remained normal except for occasional primitive cells from July, 1953, until about the end of June, 1954. During that time the patient sustained a fracture of the left cuboid bone due to a fall and a fracture of the head of the right ulna due to a wringer injury. The spleen and liver were consistently slightly enlarged. The general health was good. On July 5, 1954, the hæmoglobin value was found to be 73%, the erythrocytes were fairly well stained, and occasional macrocytes were seen. Platelets were very scanty. The leucocytes numbered 3800 per cubic millimetre, made up of band neutrophile cells 1%, neutrophile cells 18%, eosinophile cells 1%, lymphocytes 76%, "blasts" 2% and monocytes 2%. The present treatment was with "Aminopterin", 0·5 milligramme daily, and "Calvita" tablets, one three times a day. Dr. O'Keefe remarked that the boy's hair had fallen out as a result of "Aminopterin" treatment. It had grown again, but was tending to fall out once more. He asked whether the leuchæmia could be due to previous sulphonamide therapy.

Dr. J. M. Andrew emphasized the details of the onset of the illness. He said that the child had had a temperature of 105° F. and a pseudomembrane on the throat, and was apparently suffering from a typical condition of agranulocytosis. He appeared to make a complete recovery. Dr. Andrew felt that the subsequent development of leuchæmia was not connected with the first illness.

Dr. J. Josephs was of the opinion that the patient's condition was one of chronic leuchæmia in a state of recrudescence. He asked Dr. McLean how often recurrent cases of granulocytosis were really cases of leuchæmia.

Dr. McLean congratulated Dr. Andrew and Dr. O'Keefe on their management of the case. He quoted evidence to indicate that the sulphonamides had an ætiological importance in the incidence of leuchæmia. The incidence of leuchæmia had greatly increased in the United States and the United Kingdom in recent years and also in Victoria. That might be attributed to drugs and chemicals to which the community was now exposed, but the indictment of sulphonamides was purely speculative. Other factors causing damage to bone marrow (such as radiation) might be responsible. Exposure to radioactivity at Hiroshima had caused a great increase in leuchæmia there. The large number of "blast" cells in the bone marrow definitely indicated that in the present case the condition was acute. Dr. McLean said that it was impossible to differentiate the type of leuchæmia from the appearance of the "blast" cells. With regard to treatment, "Aminopterin" affected the growth of all cells. The alopecia was a toxic effect. "Aminopterin" therapy produced a remission in 60% of children, but it was rarely effective with adults. The results of "Aminopterin" therapy showed that leuchæmia was a reversible disease, and that it might be adequately treated in the future.

## Out of the Past.

*In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.*

### A NOTICE.

[From *The Sydney Morning Herald*, November 10, 1849.][1]

Dr. McCrae[2] begs to intimate to his patients, particularly to those residing in the country, that, his health being restored and his strength daily increasing, he will in future be at home for consultation between 9 and 10 in the morning, and from half past one till 3 o'clock in the afternoon.

He will give gratuitous advice between 9 and 10 a.m., to such persons as shall come furnished with notes from clergymen, or other respectable parties, stating their inability to pay a medical man: but he can only see such patients at the time specified, in consequence of his servants having been much harassed by poor people calling and demanding gratuitous advice at all hours of the day.

Syms Terrace.

## Medical Societies.

### PÆDIATRIC SOCIETY OF VICTORIA.

A meeting of the Pædiatric Society of Victoria was held on December 8, 1954, at the Royal Children's Hospital, Carlton.

#### The Use of EDTA in Lead Poisoning.

Dr. J. E. McCoy read a paper on the use of EDTA in lead poisoning. He stated that there was no satisfactory treatment of lead poisoning, the acute form of which had a high mortality. Any new therapeutic approach was worthy of

[1] From the original in the Mitchell Library, Sydney.

[2] Farquhar McCrae, M.D., died on April 20, 1850, aged forty-three years.

trial, and recently, in the United States of America, the use of a chelating agent had been advocated.

This drug was the monocalcium disodium salt of ethylenediamine tetraacetic acid (EDTA), the trade name of which was "Versenate" (Riker). When the calcium complex of EDTA was given, lead replaced calcium, since the lead chelate of EDTA was much more stable than the calcium chelate. The stable compound thus formed was water soluble, sparsely ionized and readily excreted by the kidneys, and was said to be non-toxic in spite of the extremely high levels of blood and urinary lead. It was recommended that it be used by the intravenous route as a 3% solution, in a maximum dosage of one gramme per 30 pounds, in interrupted courses not exceeding seven days.

Dr. McCoy said that recently an opportunity had arisen to try this drug in a case of chronic lead poisoning in a patient referred to Dr. Howard Williams in the Clinical Research Unit by Dr. Mona Blanch. The patient was a lad, aged eight years and eight months at the time of his admission to hospital. His previous history revealed that at the age of three years he had been admitted to hospital with encephalitis. Since that time he had had marked pica and personality changes—particularly lack of interest in playing and inability to concentrate at school. From the age of six years there were occasions when his gait seemed clumsy and he would stumble frequently.

For one month prior to admission to hospital he complained of muscle pains in his legs and of weak feet with unsteady gait.

On examination he was found to be a pale lad with marked weakness of the plantar extensors. His hæmoglobin value was 78%, reticulocytes were present in the proportion of 1·8%, stippled cells numbered 13,784 per 1,000,000 red cells, and the urine was normal chemically and microscopically. X-ray examination of the long bones showed typical osteosclerotic lines in the metaphyseal regions. The cerebrospinal fluid was normal. The blood lead content was 0·11 milligramme per 100 millilitres. The urinary lead content was 0·08 milligramme per litre, and the urinary porphyrin content 800 microgrammes per litre. The diagnosis was considered to be chronic lead poisoning with peripheral neuritis.

It was decided to treat the boy with "Versenate" given by the oral route. His weight was 60 pounds, and he was therefore given 0·5 gramme six-hourly for eight days. The urinary lead content rose rapidly to 4·3 milligrammes per litre on the second day, and the average daily excretion was 2·0 milligrammes per twenty-four hours. Over eight days a total of 16·1 milligrammes of lead was excreted, the average urinary excretion being 3·25 milligrammes per litre.

During this course of treatment the blood lead content rose to a peak of 0·25 milligramme per 100 millilitres, and the porphyrin content increased to a peak of 1500 microgrammes per litre. The hæmoglobin value remained unchanged at 78%, the number of stippled cells fell to 6600 per 1,000,000 red cells, and the proportion of reticulocytes rose to 2·2%.

During this period of treatment there were no evident side effects, and the clinical condition of the patient was unchanged. Four days after treatment the blood and urinary levels of lead fell to the pre-treatment levels, and similarly the stippled cell count and reticulocyte count reverted to their former levels.

Fourteen days after cessation of treatment the boy was still well, and there were no symptoms of toxicity. He had apparently lost his pica, his personality had improved, and he was concentrating on correspondence school lessons. At this stage a further course of "Versenate" was given for seven days by the oral route and with the same dosage as previously. The results were similar to those of the first course, and an average of 1·9 milligrammes of lead was excreted daily. Again there were no untoward side effects whatsoever. After this course of treatment, the blood and urinary lead levels returned to their former values, but the porphyrin value and stippled cell count remained at low levels. The hæmoglobin value was unchanged.

Fourteen days later, his clinical condition having remained unchanged apart from very slight diminution in the foot-drop, a third course of "Versenate" was given for seven days, this time by the intramuscular route and with the previous dosage of 0·5 gramme six-hourly on a basis of 1·0 gramme per 30 pounds of body weight. On this occasion the lead excretion was enhanced well above the previous high levels. The maximum excretion was 9·2 milligrammes on the second day, the urinary level being 14 milligrammes per litre. The intramuscular injection caused no local reaction and no excessive pain.

On discharge from hospital eight weeks after the first course of "Versenate" had been commenced, and one week after the third course had been completed, he showed no signs of toxicity. There was slight improvement in the power of the plantar extensors and he was walking well with the aid of calipers and inbuilt toe-spring. The hæmoglobin value was 78% as on his admission to hospital, and the number of stippled cells was within normal limits. X-ray examination of his bones showed no appreciable change. His personality was bright, he had completely lost his pica, his interests were those of a normal boy of his age, and he was concentrating well on his school lessons. Dr. McCoy said that he had been followed up for four months to date and had maintained this improvement. There was no recurrence of pica, but a further slight improvement in the legs had taken place.

In summary it could not be dogmatically said that the clinical improvement was not due to good nursing care, physiotherapy and orthopædic treatment. However, in this case it had been shown that "Versenate" did enhance the excretion of lead from the body, and that (as far as could be judged to date) there was no evidence of toxicity. It had also been demonstrated that "Versenate" caused a 40-fold increase in lead excretion when given by the oral route, and when given by the intramuscular route a 160-fold increase. Demonstration of the efficiency of both these routes was a valuable finding in children, in whom intravenous therapy over long periods was sometimes difficult and upsetting to the patient.

Dr. McCoy said that the experience in handling this drug in a chronic case gave encouragement to use it in future cases of acute lead poisoning; the regime planned would be to use "Versenate" intramuscularly at first and to change to the oral route when clinical improvement so indicated. Riker Laboratories, Los Angeles, had kindly supplied the "Versenate" used. Dr. D. O. Shiels, of the Public Health Department, had arranged for the chemical estimations to be done in his laboratory.

DR. H. E. WILLIAMS, in opening the discussion, said that although the drug probably did not benefit the child in the case under consideration, much experience had been gained through his treatment in assessing the limitations of the drug and the methods of administration; this would be very useful as a basis for future treatment in cases of acute lead poisoning. He said that about two to four children were admitted to the Royal Children's Hospital each year with acute lead poisoning, and in the early part of 1954 two children had died from the condition; he felt that one of them would probably have benefited from treatment with EDTA if the drug had been available.

DR. S. SHIELDS said that there was no doubt that EDTA was of value in promoting excretion of lead from the body. It would be of value in acute cases, but not in chronic cases in which large quantities of lead were stored in the bones, as that would take some years to be completely excreted. He thought that the drug should be used very carefully as the effect on iron, manganese and cobalt in the body was not known; however, it was realized that EDTA did not combine as strongly with these metals as with lead, and so probably the stores of iron, manganese and cobalt in the body would not be depleted. He went on to say that in the treatment of lead poisoning citrate was useful and could be used for a long time; rarely did it lead to acute exacerbations with encephalopathy. Thiosulphate was also very useful, but it had to be given intravenously. BAL converted mild poisoning to severe poisoning, and the only indication for its use was in the later stage when most of the lead had been excreted. Although the intravenous use of EDTA was recommended in chronic cases, the oral use was satisfactory. What effect the prolonged use of EDTA would have, especially on the kidneys, was not known.

DR. THOMAS said that after observation of the effects of EDTA in the patient presented by Dr. McCoy, twenty patients with lead poisoning occurring in industry had subsequently been treated orally with the drug. The majority of the patients had symptoms, but after thirty-six hours of treatment symptoms were less, especially colic, and after a course of treatment there was usually marked improvement. Of the twenty patients only three showed any toxic effects. Two of them complained of intense headache and one of dizziness. Dr. Thomas wondered whether EDTA could be used prophylactically over a long period in persons exposed to the lead hazard in industry.

DR. M. POWELL asked what effect EDTA had on the excretion of mercury from the body.

In reply, Dr. McCoy said that the experience so far in the use of EDTA with mercury was insufficient to give a definite opinion. He said that the drug had been used for

pink disease without toxic effects. In conclusion he said that in any case of acute lead poisoning with encephalopathy EDTA should be used intravenously at first; later administration could be by the oral route.

### The New Children's Welfare Act.

Dr. Norval Morris, Associate Professor of Criminology, gave an address in which he discussed the origins and purposes of the recently passed *Children's Welfare Act*, 1954, dealing in particular with those sections of the Act of significance to pædiatricians. He pointed out that though child welfare legislation was administered by the Children's Welfare Department, that department actually performed something less than 15% of the actual work to be carried out under the legislation; the bulk of it was undertaken by various voluntary, mainly denominational, associations. An important purpose of the new Act was more efficiently to blend the work of the State Department and the voluntary associations.

Dr. Phyllis Tewsley discussed facilities for the care of State wards. She stated that it was not possible to discuss the practical applications of the new *Children's Welfare Act* until it was known what the regulations would be and how it would be implemented. The Act would certainly open the way to fill gaps which existed in the present system.

Facilities for the care of children who had been removed from their homes varied in different countries. In England, the emphasis was on foster home placement for children who were in need of care and protection, and 42% of the children who were in the care of local authorities were in foster homes. The second most favoured placement was the family group home. In a small, ordinary house, eight to twelve children lived with a resident house mother as a normal family. The ages ranged from three to sixteen years or more, and the children were of both sexes in most cases. The children went out to school, mixed with the neighbouring children, and joined in all local activities such as boy scouts, girl guides, church choirs *et cetera*. For the children who could not be placed in foster homes, there were provided nurseries, classification centres, hostels for maladjusted children and centres for short stay. The homes which took under thirty children were preferred. Where the homes were larger, in some cases they were being divided up into cottages or flats. The Home Office provided institutions throughout England for delinquent children. For those there were remand homes, approved schools, Borstals and detention centres. In England, the house parents did a special course of training arranged by the Home Office, and trained nursery nurses were used extensively with the younger children. Each county had many field officers, who worked under the children's officer, supervising placements, finding foster homes and assisting problem families. In the delinquent field, paid trained probation officers investigated all cases of delinquency which came before the Children's Court; they also helped and advised children remaining at home, and their parents.

In Victoria, all children in need of care and protection, and all delinquents passed through a central depot at Royal Park, run by the State. From there they went to institutions, which were run by voluntary organizations, or to foster homes.

Dr. Tewsley said that at the present time at the depot at Royal Park, there was a total of 208 children, made up in the following way: 27 on remand, 16 habitual absconders, 36 physically handicapped, 115 awaiting placement. If they were divided according to age there were 17 babies to two years of age, 60 pre-school children over two years of age, 29 school-age girls, 69 school-age boys and 43 over school age. If they were classified according to behaviour there were eight on charges of being neglected and 19 on charges of minor crimes. Wards of the State included 138 in need of care and protection, 16 habitual absconders and 27 delinquents.

Discussing the placement of children from Royal Park, Dr. Tewsley said that, first, the children could go to foster parents, or they could be either adopted or "boarded out", and second they could go to institutions run by voluntary organizations. They were placed according to their religion in appropriate homes. The Child Welfare Department of Victoria had no institution other than the one at Royal Park. New South Wales had 23 institutions run by the State for its wards, and South Australia 11. The main difficulties in the way of placement were that many children were not available to foster parents, as their own parents were still interested in the children and paying towards their upkeep, and children were more frequently accompanied by siblings than alone. It was less easy to find a foster home for two children and impossible for nine children. There were no "homes" taking children of both sexes and all ages including babies. Children such as the physically handicapped child, the subnormal child, the delinquent or first offender over fourteen years old, habitual absconders, maladjusted children and delinquent girls were very difficult to place. For the last five groups, there were either no institutions or the number was insufficient.

Under the new Act, some new institutions might be started to fill in the existing gaps. A centre for delinquent girls had already been built by the Government at Nunawading. There might also be an increased field staff and a system of in-service training.

Dr. H. Boyd Graham said that he had been interested in the problem over a period of years, and that most pædiatricians were interested in all aspects involved in the care of children. He said that when the Act was proclaimed he thought that the Royal Children's Hospital or the Pædiatric Society of Victoria should make strong representation to the Minister to have a member or members elected to the advisory council committee which was to be set up.

Dr. M. Lane asked Professor Morris if the child who was not attending school could not be dealt with by sections provided in the *Educational Act*.

In reply, Professor Morris said as far as he knew the only power provided for by the *Educational Act* was for temporary placement of the child. In the present Bill there would be power by the State to confine such children up to the age of eighteen years, and that could be extended if necessary to the age of twenty-one years.

Dr. Dora Bialestock asked what was the function of the voluntary visitor.

In reply, Professor Morris said that he thought that the voluntary visitor would carry out a similar function to those people visiting mental institutions.

Dr. J. Colebatch agreed with Dr. Boyd Graham that members of the Royal Children's Hospital and the Pædiatric Society of Victoria should seek representation on the advisory council committee. He asked Professor Morris what facilities and finance would be available for training regional officers.

In reply, Professor Morris said that he thought that the training should be similar to that of a social worker with special practical training in field work. Facilities for training and finance had not been determined at the present stage. He said that in New South Wales about 95 field officers were functioning in most country areas, and it was intended to appoint one in the South Melbourne district early in the new year.

Dr. Colebatch asked Dr. Tewsley what was the difficulty in obtaining foster parents in Victoria when such people were readily available in England.

In reply, Dr. Tewsley said that there was no one in Victoria searching for foster homes, and the country areas were untapped. She did not know what financial assistance would be given to foster parents.

Dr. John Williams asked if the new Act was going to make it any easier for children to obtain adequate care when it was needed.

In reply, Professor Morris said that one of the advantages of the Act was that more money should be available for institutions, and consequently more help should be forthcoming for needy children.

On the motion of Dr. J. Williams, seconded by Dr. A. Derham, it was decided that a letter be sent to the Minister urging that a member of the Pædiatric Society of Victoria be appointed to the advisory council committee when it was established.

## Medical Practice.

### THE POISONS ACT, 1928, OF VICTORIA.

The following proclamation is published in the *Victoria Government Gazette*, Number 159, of April 6, 1955.

PROCLAMATION.

By His Excellency the Governor of the State of Victoria and its Dependencies in the Commonwealth of Australia, etc.

Whereas by section thirty-eight of the *Poisons Act* 1928 as amended by section five of the *Poisons Act* 1930, power

is conferred on the Governor in Council by Proclamation, on the recommendation of the Pharmacy Board of Victoria, to add to paragraph (2) of the Sixth Schedule to the *Poisons Act* 1928 the name of any substance or preparation the name of which is not included in paragraph (1) of the said Schedule, but which is likely to be productive, if improperly used, of ill-effects of such a nature as to make it expedient in the opinion of the Board to add the name thereof to the said paragraph (2) and to declare that Division 2 of Part III. of the said Poisons Act shall apply to the said substance or preparations in the same manner as it applies to the substances or preparations included in the said paragraph (2):

And whereas the names of the substances and preparations—

(1) Anti-cholinesterase substances (other than Di-isopropyl fluorophosphonate whether described as D.F.P. or any other name) such as neostigmine, their salts, derivatives, preparations and admixtures by whatever name such substances are described; and

(2) Anti-parkinsonian substances (other than Trihexyphenidyl (3-(1-piperidyl)-1-phenyl-1-cyclo-hexyl-1-propanol hydrochloride) whether described as Artane or any other name) whether described as Ethopropazine, Diethazine, Procyclidine, Caramiphen, Pagitane or any other name,

(hereinafter referred to as the aforesaid substances and preparations) are not specifically included in paragraph (1) of the said Schedule but are likely to be productive, if improperly used, of ill-effects of such a nature as to make it expedient in the opinion of the said Board to add the names thereof to the said paragraph (2) of the Sixth Schedule:

Now therefore I, the Governor of the State of Victoria in the Commonwealth of Australia, by and with the advice of the Executive Council of the said State and on the recommendation of the said Board, do by this my Proclamation add the names of the aforesaid substances and preparations to paragraph (2) of the Sixth Schedule to the said Act by adding to the name of the substance or preparation—

"Di-isopropyl fluorophosphonate whether described as D.F.P. or any other name";

the further words—

"and other anti-cholinesterase substances such as neostigmine, their salts, derivatives, preparations and admixtures by whatever name such substances are described",

and in the name of the substance and preparation—

"Trihexyphenidyl (3-(1-piperidyl)-1-phenyl-1-cyclo-hexyl-1-propanol hydrochloride) whether described as Artane or any other name",

by adding—

(*a*) after "Trihexyphenidyl" the expression (benzhexol hydrochloride)",

(*b*) after the word "hydrochloride" the words "and other anti-parkinsonian substances", and

(*c*) after the word "Artane" the words Ethopropazine, Diethazine, Procyclidine, Caramiphen, Pagitane",

and declare that the provisions of Division 2 of Part III. of the *Poisons Act* 1928 shall apply to the aforesaid substances and preparations so added to paragraph (2) of the Sixth Schedule to the *Poisons Act* 1928 in the same manner as it applies to the substances and preparations included in the said paragraph (2).

Given under my Hand and the Seal of the State of Victoria aforesaid, at Melbourne, this twenty-ninth day of March, in the year of our Lord One thousand nine hundred and fifty-five, and in the fourth year of the reign of Her Majesty Queen Elizabeth II.

(L.S.) DALLAS BROOKS.

By His Excellency's Command,

WM. BARRY,
Minister of Health.

# Correspondence.

## AN UNUSUAL CASE OF IRITIS.

SIR: We are indebted to F. K. Bartlett in the journal of April 9 for his autobiographical report of the treatment of non-purulent, non-specific iritis by the use of chloramphenicol. Those of us who have worked in country districts where such cases cannot be referred to clinics will welcome this ray of hope in our futility. Many cases hang on indefinitely in spite of all treatment. There is another line of treatment which I have found very helpful in the limited number of cases I have handled during the last twelve years. The first case had had eighteen months' orthodox treatment at various eye clinics, and the recurrences were as frequent and as distressing as at first. Searching for some unorthodox line of attack, it occurred to me that this might be a neuritis rather than a specific iritis. I therefore started a course of vitamin $B_1$ injections with phenobarbitone orally. This treatment was eminently successful. Since then, five other cases have been treated with equal success. These were all cases of long standing; no cases of early iritis have been seen.

In the case of bilateral iritis—if such occurs—an allergic origin could be considered. The combination of the above two lines of treatment could be used in resistant iritis.

Yours, etc.,

P. L. DANIEL.
111 Anzac Parade,
Kensington,
New South Wales.
April 14, 1955.

## EXHIBITION OF DOCTORS' HOBBIES.

SIR: One of the incidental but attractive features of the Australasian Medical Congress to be held at the University of Sydney on August 20 to 27, 1955, will be the exhibition of doctors' hobbies.

At previous Congresses visitors have been entertained with a varied display, in which the hobbies ranged from toy-making to fashioning of medical tools, whilst some members showed their talent in the arts.

As organizers of the hobbies exhibition, we are particularly anxious that it should equal at least, if not surpass, previous displays, and we feel sure that the response from the members of Congress will accomplish this. We ask, however, that all members who desire to participate communicate with one of us as soon as possible.

Yours, etc.,

GRANT LINDEMAN,
Chairman.
M. ELLIOT-SMITH,
Member, Hobbies Committee.
Australasian Medical Congress (British Medical Association),
135 Macquarie Street,
Sydney.
April 21, 1955.

## YOUNG DOCTORS AND SPECIALIZATION.

SIR: I would appreciate the opportunity of replying to the Latinizer who has joined in our controversy (April 9, 1955).

My remarks have been misconstrued. In my original letter I stated: "In the field of general medicine there is need for some attempt to gain general practice experience, but in the various surgical fields, and the highly specialized medical fields, valuable time would be lost."

It is obvious that I do not regard general practice experience, prior to specialization, as completely useless. Many years in general practice would certainly be most enlightening and perhaps make some specialists nice doctors with charming and sympathetic dispositions. But, after all, the capacity to understand human nature with its faults and foibles is often something inherent in most of us. A charming and understanding nature does not make a good surgeon, although it is a social asset.

If I should develop a carcinoma of the rectum, I will not be seeking a nice surgeon, but the best surgeon for the job. Even Mrs. Jones would be able to appreciate that this is common sense. The best surgeon is the best trained and most highly experienced man for the job. Shaw could appreciate the problem in question when he stated: "There are only two qualities in the world, efficiency and inefficiency; and only two sorts of people, the efficient and the inefficient." Efficiency in the specialized fields of modern medicine can only be achieved by early and intense training.

Most young Australian specialists have had quite reasonable experience in many branches of medicine in large teaching hospitals before proceeding to their post-graduate training. Efficiency in one particular field is then developed during the ensuing years of post-graduate study.

I certainly consider that the young specialist-to-be should be familiar with the practical aspects of most branches of medicine, including psychology.

A big proportion of specialists who have not spent many years in general practice retain their inherent capacity to understand their fellow man. On the other hand we can find many disgruntled overworked general practitioners who are finding it increasingly difficult to understand and sympathize with many of the patients who prolong their day's work unnecessarily.

*"Ne tentes . . ."* cannot appreciate the difficulties which many patients create for their doctors. Perhaps the specialist whom *"Ne tentes . . ."* originally attended was, after all, quite an understanding and sympathetic person, but the limits of these virtues might have been exceeded by the demands of a difficult patient.

"The inside of a little human being" may not have changed over the æons of time, but his outlook has certainly altered. Nowadays patients expect, and often demand, the best specialized treatment available. This can only be obtained by close cooperation between general practitioner and specialist, for each has a distinct role to play. Clinics like the Mayo and the Lahey represent the specialized outlook. Surely such is the only way to achieve complete efficiency. Even in Australia we find everywhere the development of clinics with general practitioners and specialists combining to produce greater and greater efficiency in their respective fields.

The "jet age specialist" will always draw patients provided he gives the most efficient service. He may not fully appreciate the domestic problems of Mrs. Jones, but at least he will know how to deal with the lower end of her alimentary tract in the most expert fashion. She will be confident in the knowledge that her specialist is a good one. If her general practitioner is also a good one, what better combination can *"Ne tentes . . ."* suggest? Perhaps this modern medical unit (general practitioner *plus* specialist) is the system which is best described by *"Ne tentes, aut perfice"*.

Yours, etc.,

Brisbane,
April 18, 1955.

DANIEL LANE.

## A CANCER DETECTION AND PREVENTION CLINIC

SIR: Dr. Graham Crawford's article about "A Cancer Detection and Prevention Clinic" was of considerable interest, particularly as there have been two so-called cancer detection clinics operating in Tasmania since 1952. It is obvious from the article that Dr. Crawford's clinic is well organized and well staffed.

In Tasmania the staff at each clinic consists of one doctor and one sister, and laboratory facilities are available for the routine urine tests and Papanicolau smears. A twenty-minute period is allowed each patient, in which time a history and examination has to be conducted. Cases with non-malignant lesions are advised to seek medical treatment. Over the three years that these clinics have been in existence, several thousand people have been examined, and several cases only of cancer have been detected (latest figures not yet published), mainly by palpation rather than by any special technique.

The point which I wish to emphasize is that for a so-called cancer detection clinic to perform the function expected of it by the public, it must thoroughly investigate every system of the body by clinical, pathological, radiological and endoscopic means. In practice this would be extremely expensive, and for that reason almost impracticable. At present the clinics in Tasmania, and also Dr. Crawford's clinic I would think, thoroughly examine only the breasts, skin, mouth, anus and cervix, and therefore they should not claim to detect cancer in any organs other than these few.

To label such clinics as cancer detection clinics gives a quite unwarranted impression to the public, and also gives a dangerous sense of security to anyone who has attended and has been informed that no cancer was detected. I consider that if such clinics must be run, they must be extremely elaborate institutions with multiple investigations, or they must publicly limit themselves to cancer detection in a few superficial organs only. Cancer detection should be an all-or-nothing affair, not a "half-baked" scheme instituted mainly for the sake of appearance.

From experience in one of the Tasmanian clinics over several years I firmly believe that cancer detection clinics are not desirable, particularly because they pretend to do that which they cannot do thoroughly. Education of the public to have regular medical examinations, together with reminders to the medical practitioners of the important features in cancer detection, and the availability of good laboratory facilities to all doctors, are the avenues from which the best results will be obtained.

Yours, etc.,

174 Macquarie Street,
Hobart,
April 15, 1955.

FRANKLIN R. FAY.

## DOCTORS' NAMES IN THE TELEPHONE DIRECTORY.

SIR: The proposal for doctors' names to be grouped under suburbs in the classified telephone directory needs careful consideration. Such a scheme would tend to confine a practice to the suburb in which the surgery is located. Yet owing to the way the geographical boundaries are often drawn, the major part of the practice may be in one or more adjacent suburbs.

Should such a scheme become established, doctors would ever after be forced to pay an anual fee of £1 10s. (in many cases £2 10s.); otherwise their names would be omitted from the list, almost tantamount to self-deregistration.

Such a scheme would be of benefit only to the public, not to the doctors listed. If the Postmaster-General wants to draw up such lists for public convenience, the cost should be met by the department, certainly not by the doctors.

In the event of some doctors refusing to participate, would the doctors who did participate be obtaining the unfair advantage of paid advertisement? Would it be ethical?

Yours, etc.,

Waverley,
New South Wales,
April 16, 1955.

W. T. WHITBY.

# Post-Graduate Work.

## THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

### Annual Subscription Course.

THE Post-Graduate Committee in Medicine in the University of Sydney announces that Major-General F. Kingsley Norris, C.B., C.B.E., D.S.O., E.D., M.D., Director-General of Medical Services, will give a lecture on "Medical Problems of Atomic Warfare" on Tuesday, May 24, 1955, at 8.15 p.m., in the Stawell Hall, 145 Macquarie Street, Sydney. This lecture is being given during the annual general revision course and is included in the annual subscription course.

# Naval, Military and Air Force.

## APPOINTMENTS.

THE undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 11, of March 3, 1955.

AUSTRALIAN MILITARY FORCES.

### Citizen Military Forces.

*Northern Command.*

***Royal Australian Army Medical Corps (Medical).***—1/39164 Captain (provisionally) I. R. Ferguson is seconded for post-graduate studies in the United Kingdom, 15th November, 1954.

*Central Command.*

*Royal Australian Army Medical Corps (Medical).*—4/35217 Major F. B. Turner relinquishes the temporary rank of Lieutenant-Colonel and is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (Central Command), 8th January, 1955.

*Tasmania Command.*

*Royal Australian Army Medical Corps (Medical).*—The provisional ranks of the following officers are confirmed: Captains 6/15379 K. S. Millingen and 6/15251 J. C. S. Officer.

**Reserve Citizen Military Forces.**

*Royal Australian Army Medical Corps.*

*1st Military District.*—The following officers are retired, 14th October, 1954: Honorary Captains A. G. S. Cooper, E. W. Finkle and N. F. George.

*To be Honorary Captains, 25th January,* 1955.—Ralph Lionel Hockin, Bruce Kynaston and Bryan Watson Brown.

*3rd Military District.*—The following officers are retired, 14th December, 1954: Honorary Lieutenant-Colonel Sir F. M. Burnet, Honorary Majors A. R. Hamilton and R. L. Naylor, Honorary Captains J. M. Andrew, G. R. Bearham, J. A. Broben, G. R. Davidson, A. G. Gault, W. R. D. Griffiths, T. A. F. Heale, L. S. Horton, L. L. Lovett, J. B. G. Muir and A. Oldham.

*4th Military District.*—The following officers are retired, 13th December, 1954: Honorary Captains H. H. Hurst and H. F. Hustler.

*5th Military District.*—Honorary Major G. Oxer is retired, 18th October, 1954.

*6th Military District.*—Honorary Major B. Hiller is retired, 12th October, 1954.

The following officers are placed upon the Retired List within Military Districts and on the dates as shown, with permission to retain their rank and wear the prescribed uniform:

*1st Military District.*—Captains G. J. Byrne, T. M. S. Hall and A. J. May, 14th October, 1954.

*2nd Military District.*—Lieutenant-Colonel J. H. Halliday, Major (Honorary Lieutenant-Colonel) E. Murray-Will, M.B.E., Majors C. H. W. Lawes and B. Moore, and Captain (Honorary Major) R. Jeremy, 12th November, 1954.

*3rd Military District.*—Lieutenant-Colonels (Honorary Colonels) J. B. Colquhoun and G. A. Penington, E.D., Majors J. H. Niall and J. F. Williams, Captains R. H. Boyt, H. C. R. Carter, S. K. Crownson, G. Forsyth, A. J. MacDonald and K. H. McFarlane, and Lieutenant (Honorary Captain) K. H. Hadley, 14th December, 1954.

*4th Military District.*—Captains (Honorary Majors) S. W. Fewell and H. A. McCoy, 13th December, 1954.

*5th Military District.*—Major (Honorary Lieutenant-Colonel) J. P. Ainslie, Majors A. P. Davis and C. R. Dunkley, and Captains A. M. Murphy and J. M. O'Donnell, 18th October, 1954.

ROYAL AUSTRALIAN AIR FORCE.

*Air Force Reserve: Medical Branch.*

The following are appointed to a commission with the rank of Flight Lieutenant: David Wyndham Quin (257923), 13th October, 1954; William Warwick John Liddle (277629), 16th November, 1954.

Flight Lieutenant (Temporary Squadron Leader) A. H. Penington (251211) is promoted to the temporary rank of Wing Commander, 27th October, 1954.

# Medical Prizes.

## THE MEDICAL WOMEN'S SOCIETY OF NEW SOUTH WALES ANNUAL PRIZE.

THE following are details of the Medical Women's Society of New South Wales Annual Prize:

1. The Medical Women's Society of New South Wales shall award a prize of the value of 25 guineas, open to any medical woman registered in New South Wales.

**DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED APRIL 9, 1955.[1]**

| Disease. | New South Wales. | Victoria. | Queensland. | South Australia. | Western Australia. | Tasmania. | Northern Territory.[2] | Australian Capital Territory. | Australia.[3] |
|---|---|---|---|---|---|---|---|---|---|
| Acute Rheumatism | .. | 2(1) | 1 | .. | .. | .. | .. | .. | 3 |
| Amœbiasis | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Ancylostomiasis | 1(1) | .. | .. | .. | .. | .. | .. | .. | 1 |
| Anthrax | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Bilharziasis | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Brucellosis | .. | 1 | .. | .. | 1(1) | .. | .. | .. | 2 |
| Cholera | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Chorea (St. Vitus) | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Dengue | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Diarrhœa (Infantile) | 3(2) | 17(16) | 1(1) | .. | .. | .. | .. | 4 | 25 |
| Diphtheria | .. | 3(3) | .. | .. | 2(2) | .. | .. | .. | 5 |
| Dysentery (Bacillary) | .. | .. | 3(1) | .. | 4(3) | .. | .. | .. | 7 |
| Encephalitis | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Filariasis | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Homologous Serum Jaundice | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Hydatid | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Infective Hepatitis | 30(10) | 49(37) | .. | 4(1) | 2 | .. | .. | .. | 85 |
| Lead Poisoning | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Leprosy | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Leptospirosis | .. | .. | 5 | .. | .. | .. | .. | .. | 5 |
| Malaria | .. | .. | 1(1) | .. | .. | .. | .. | .. | 1 |
| Meningococcal Infection | 1 | 1(1) | 1 | .. | .. | .. | .. | .. | 3 |
| Ophthalmia | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Ornithosis | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Paratyphoid | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Plague | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Poliomyelitis | 8(3) | 4(3) | 9(3) | 6(3) | .. | .. | .. | .. | 27 |
| Puerperal Fever | 2 | .. | .. | .. | .. | .. | .. | .. | 2 |
| Rubella | .. | 2(1) | .. | 1 | 1(1) | .. | .. | .. | 4 |
| Salmonella Infection | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Scarlet Fever | 7(4) | 21(13) | 2(1) | 3(2) | 1(1) | .. | .. | .. | 34 |
| Smallpox | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Tetanus | .. | .. | 1(1) | .. | .. | .. | .. | .. | 1 |
| Trachoma | .. | .. | .. | .. | 4 | .. | .. | .. | 4 |
| Trichinosis | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Tuberculosis | 26(22) | 10(8) | .. | 8(7) | 8(6) | 3(1) | .. | .. | 55 |
| Typhoid Fever | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Typhus (Flea-, Mite- and Tick-borne) | .. | .. | 2 | .. | .. | .. | .. | .. | 2 |
| Typhus (Louse-borne) | .. | .. | .. | .. | .. | .. | .. | .. | .. |
| Yellow Fever | .. | .. | .. | .. | .. | .. | .. | .. | .. |

[1] Figures in parentheses are those for the metropolitan area.

[2] Figures not available.

[3] Figures incomplete owing to absence of returns from Northern Territory.

2. The prize shall be awarded for an original contribution on a subject of medical interest published or ready for publication during that year.

3. In the event of a contribution by two or more medical women in collaboration the prize shall be divided equally between the contributors. Work done in collaboration with other than medical women may be submitted.

4. The Medical Women's Society of New South Wales shall appoint examiners, and the award will be made on their recommendation in the month of February each year.

5. The closing date for entries shall be November 30 of each year.

6. The prize shall not be awarded if either the examiners or the committee of the Society consider that the standard of the work or works is not sufficiently high to justify the award of the prize.

## Australian Medical Board Proceedings.

### NEW SOUTH WALES.

THE following have been registered, pursuant to the provisions of the *Medical Practitioners Act*, 1938-1953, as duly qualified medical practitioners: Peeke, Ronald Keith, M.B., B.S., 1951 (Univ. Melbourne); Elyan, Michael, L.L.M., R.C.P. (Ireland), 1921, L.L.M., R.C.S. (Ireland), 1921, D.C.H., 1949; Reid, James Campbell, M.B., Ch.B., 1932 (Univ. Glasgow), F.R.C.S.I., 1951.

The following additional qualifications have been registered: Hercus, Victor Macky (M.B., B.S., 1942, Univ. Sydney), M.R.C.P. (Edinburgh), 1953, D.A. (London), 1954; McMahon, Leo Hanney (M.B., 1939, Univ. Sydney), D.G.O., 1950 (Univ. Sydney); Murphy, John Denis (M.B., B.S., 1945, Univ. Sydney), M.R.A.C.P., 1954.

## Nominations and Elections.

THE undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

Banfield, John Francis, M.B., B.S., 1948 (Univ. Sydney), 239 Gosford Road, The Entrance, New South Wales.

The undermentioned have been elected as members of the New South Wales Branch of the British Medical Association: Bell, David Samuel, M.B., B.S., 1955 (Univ. Sydney); Cable, Ronald Hughes, M.B., B.S., 1955 (Univ. Sydney); Channon, Pamela, M.B., B.S., 1955 (Univ. Sydney); Fitzgerald, Ronald Robert, M.B., B.S., 1955 (Univ. Sydney); Johnson, Frank Louis, M.B., B.S., 1955 (Univ. Sydney); Klein, Douglas George, M.B., B.S., 1955 (Univ. Sydney); Gemenis, Cedric Matthew, M.B., B.S., 1954 (Univ. Sydney); House, Harry, M.B., B.S., 1954 (Univ. Sydney); Fisher, Roderick William, M.B., B.S., 1952 (Univ. Sydney); Halliday, Edward James, M.B., B.S., 1944 (Univ. Sydney); McCouat, John Battson, M.B., B.S., 1953 (Univ. Sydney); Moore, Keith Patrick William, M.B., B.S., 1952 (Univ. Sydney); Ofner, Francis, registered in accordance with the provisions of Section 17 (1) (c) of the *Medical Practitioners Act*, 1938-1953.

## Deaths.

THE following death has been announced:

LILLEY.—Charles Mitford Lilley, on April 16, 1955, at Brisbane.

## Medical Appointments.

Dr. J. S. Rogers has been appointed honorary clinical assistant to the ophthalmological department in the Royal Adelaide Hospital.

Dr. Joyce Margaret Bullock has been appointed medical officer to State Hospitals and Homes in the Department of Public Health, New South Wales.

Dr. Betty Marjorie Lowe has been appointed to the School Medical Service in the Department of Public Health, New South Wales.

Dr. H. R. Bailey has been appointed Assistant Director of Psychiatric Clinical Services in the Division of Mental Hygiene, Department of Public Health, New South Wales.

Dr. Merna Alma Mueller has been appointed officer of health at and around Fowler's Bay, Penong, Cook and Tarcoola, South Australia.

Dr. Ronald Lewis Clayfield has been appointed a quarantine officer at Portland, Victoria, under the provisions of the *Quarantine Act*, 1908-1950.

Dr. J. L. Evans has been appointed a psychiatrist in the Department of Public Health of New South Wales.

Dr. S. A. Mellick has been appointed part-time government medical officer in the Department of Health and Home Affairs, Brisbane.

Dr. H. M. Fisher has been appointed to the board of the Queen Victoria Maternity Hospital, Launceston, as the representative of the Queen Victoria Maternity Hospital Association.

## Diary for the Month.

MAY 3.—New South Wales Branch, B.M.A.: Organization and Science Committee.
MAY 4.—Victorian Branch, B.M.A.: Clinical Meeting.
MAY 4.—Western Australian Branch, B.M.A.: Branch Council.
MAY 6.—Queensland Branch, B.M.A.: General Meeting.
MAY 10.—New South Wales Branch, B.M.A.: Executive and Finance Committee.

## Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

*New South Wales Branch* (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

*Queensland Branch* (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

*South Australian Branch* (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

*Western Australian Branch* (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all contract practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

## Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

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